NW., Washington, DC 20420 (202) 233–3021.

Comments and questions about the items on the list should be directed to VA's OMB Desk Officer, Joseph Lackey, NEOB, room 3002, Washington, DC 20503, (202) 395–7316. Do not send requests for benefits to this address.

DATES: Comments on the information collection should be directed to the OMB Desk Officer within 30 days of this notice.

Dated: November 9, 1993.

By direction of the Secretary.

B. Michael Berger,

Director, Records Management Service.

Extension

1. Application for Educational Assistance Test Program Benefits (Section 901, Pub. L. 96–342), VA Form 22–8889.

2. The form is used by individuals under the Educational Assistance Test Program to apply for educational benefits. The information is used by VA to determine eligibility for benefits.

3. Individuals or households.

4. 175 hours.

5. 30 minutes.

6. On occasion.

7. 350 respondents.

[FR Doc. 93–28696 Filed 11–22–93; 8:45 am]

BILLING CODE 8320–01–M

Information Collection Under OMB Review: Report of Accidental Injury in Support of Claim for Compensation or Pension, VA Form 21–4176

AGENCY: Department of Veterans Affairs.

ACTION: Notice.

The Department of Veterans Affairs has submitted to OMB the following proposal for the collection of information under the provisions of the Paperwork Reduction Act (44 U.S.C. chapter 35). This document lists the following information:

(1) The title of the information collection, and the Department form number(s) if applicable;

(2) A description of the need and its use;

(3) Who will be required or asked to respond;

(4) An estimate of the total annual reporting hours, and recordkeeping burden, if applicable;

(5) The estimated average burden hours per respondent;

(6) The frequency of response; and

(7) An estimated number of respondents.

ADDRESSES: Copies of the proposed information collection and supporting documents may be obtained from Janet G. Byers, Veterans Benefits Administration (20A5), Department of Veterans Affairs, 810 Vermont Avenue, NW., Washington, DC 20420 (202) 233–3021.

Comments and questions about the items on the list should be directed to VA's OMB Desk Officer, Joseph Lackey, NEOB, room 3002, Washington, DC 20503, (202) 395–7316. Do not send requests for benefits to this address.

DATES: Comments on the information collection should be directed to the OMB Desk Officer within 30 days of this notice.

Dated: November 9, 1993.

By direction of the Secretary.

B. Michael Berger,

Director, Records Management Service.

Revision

1. Report of Accidental Injury in Support of Claim for Compensation or Pension, VA Form 21–4176.

2. The form is used to obtain information regarding accidents resulting in the disability upon which a claim is based and to give the veteran an opportunity to provide information based on his/her own knowledge regarding the accident. The information is used by VA in determining eligibility for benefits.

3. Individuals or households.

4. 2,200 hours.

5. 30 minutes.

6. On occasion.

7. 4,400 respondents.

[FR Doc. 93–28698 Filed 11–22–93; 8:45 am]

BILLING CODE 8320–01–M

Information Collection Under OMB Review: Report of Automatic Manufactured Home and/or Lot Loan, VA Form 26–8149

AGENCY: Department of Veterans Affairs.

ACTION: Notice.

The Department of Veterans Affairs has submitted to OMB the following proposal for the collection of information under the provisions of the Paperwork Reduction Act (44 U.S.C. chapter 35). This document lists the following information: (1) The title of the information collection, and the Department form number(s), if applicable; (2) a description of the need and its use; (3) who will be required or asked to respond; (4) an estimate of the total annual reporting hours, and recordkeeping burden, if applicable; (5) the estimated average burden hours per respondent; (6) the frequency of response; and (7) an estimated number of respondents.

ADDRESSES: Copies of the proposed information collection and supporting documents may be obtained from Janet G. Byers, Veterans Benefits Administration (20A5), Department of Veterans Affairs, 810 Vermont Avenue, NW., Washington, DC 20420, (202) 233–3021.

Comments and questions about the items on the list should be directed to VA's OMB Desk Officer, Joseph Lackey, NEOB, room 3002, Washington, DC 20503, (202) 395–7316. Do not send requests for benefits to this address.

DATES: Comments on the information collection should be directed to the OMB Desk Officer by December 23, 1993.

Dated: November 9, 1993.

By direction of the Secretary.

B. Michael Berger,

Director, Records Management Service.

Extension

1. Report of Automatic Manufactured Home and/or Lot Loan, VA Form 26–8149.

2. The form is used by lenders authorized to make manufactured home and/or lot loans on the automatic basis. The information is used by VA to determine that all requirements are met before issuing evidence of guaranty.

3. Businesses or other for-profit—Small business or organizations.

4. 39 hours.

5. 30 minutes.

6. On occasion.

7. 78 respondents.

[FR Doc. 93–28702 Filed 11–22–93; 8:45 am]

BILLING CODE 8320–01–M

Information Collection Under OMB Review: Request for Verification of Employment, VA Form 26–8497

AGENCY: Department of Veterans Affairs.

ACTION: Notice.

The Department of Veterans Affairs has submitted to OMB the following proposal for the collection of information under the provisions of the Paperwork Reduction Act (44 U.S.C. chapter 35). This document lists the following information: (1) The title of the information collection, and the Department form number(s), if applicable; (2) a description of the need and its use; (3) who will be required or asked to respond; (4) an estimate of the total annual reporting hours, and recordkeeping burden, if applicable; (5) the estimated average burden hours per respondent; (6) the frequency of response; and (7) an estimated number of respondents.

ADDRESSES: Copies of the proposed information collection and supporting documents may be obtained from Janet G. Byers, Veterans Benefits Administration (20A5), Department of Veterans Affairs, 810 Vermont Avenue, NW., Washington, DC 20420 (202) 233–3021.

Comments and questions about the items on the list should be directed to VA's OMB Desk Officer, Joseph Lackey, NEOB, room 3002, Washington, DC 20503, (202) 395–7316. Do not send requests for benefits to this address.

DATES: Comments on the information collection should be directed to the OMB Desk Officer by December 23, 1993.

Dated: November 9, 1993.

By direction of the Secretary.

B. Michael Berger,

Director, Records Management Service.

Extension

1. Request for Verification of Employment, VA Form 26–8497
2. The form is used by lenders to verify a loan applicant's income and employment information when making guaranteed and insured loans. The use of this form is optional since any comprehensible form of independent verification is acceptable, provided all information contained on VA Form 26–94497 is furnished.
3. Business or other for-profit
4. 52,667 hours.
5. 10 minutes.
6. On occasion.
7. 316,000 respondents.

[FR Doc. 93–28699 Filed 11–22–93; 8:45 am]

BILLING CODE 8320–01–M

Information Collection Under OMB Review: Application for Release From Personal Liability to the Government on a Home Loan, VA Form 26–6381

AGENCY: Department of Veterans Affairs.

ACTION: Notice.

The Department of Veterans Affairs has submitted to OMB the following proposal for the collection of information under the provisions of the Paperwork Reduction Act (44 U.S.C. chapter 35). This document lists the following information: (1) The title of the information collection, and the Department form number(s), if applicable; (2) a description of the need and its use; (3) who will be required or asked to respond; (4) an estimate of the total annual reporting hours, and recordkeeping burden, if applicable; (5) the estimated average burden hours per respondent; (6) the frequency of response; and (7) an estimated number of respondents.

ADDRESSES: Copies of the proposed information collection and supporting documents may be obtained from Janet G. Byers, Veterans Benefits Administration (20A5), Department of Veterans Affairs, 810 Vermont Avenue, NW., Washington, DC 20420 (202) 233–3021.

Comments and questions about the items on the list should be directed to VA's OMB Desk Officer, Joseph Lackey, NEOB, room 3002, Washington, DC 20503, (202) 395–7316. Do not send requests or benefits to this address.

DATES: Comments on the information collection should be directed to the OMB Desk Officer by December 23, 1993.

Dated: November 9, 1993.

By direction of the Secretary.

B. Michael Berger,

Director, Records Management Service.

Extension

1. Application for Release from Personal Liability to the Government on a Home Loan, VA Form 26–6381
2. The form is completed by veterans who are selling their VA-guaranteed homes by assumption rather than requiring the purchaser to obtain their own financing to pay off the loan. The information is used by VA to determine assumption approval.
3. Individuals or households—Businesses or other for-profit.
4. 1,328 hours.
5. 10 minutes.
6. On occasion.
7. 7,973 respondents.

[FR Doc. 93–28700 Filed 11–22–93; 8:45 am]

BILLING CODE 8320–01–M

Information Collection Under OMB Review: Request to Lender for Status of Loan Account-LCS, VA Form 26–8778

AGENCY: Department of Veterans Affairs.

ACTION: Notice.

The Department of Veterans Affairs has submitted to OMB the following proposal for the collection of information under the provisions of the Paperwork Reduction Act (44 U.S.C. chapter 35). This document lists the following information:

(1) The title of the information collection, and the Department form number(s), if applicable;

(2) A description of the need and its use;

(3) Who will be required or asked to respond;

(4) An estimate of the total annual reporting hours, and recordkeeping burden, if applicable;

(5) The estimated average burden hours per respondent;

(6) The frequency of response; and

(7) An estimated number of respondents.

ADDRESSES: Copies of the proposed information collection and supporting documents may be obtained from Janet G. Byers, Veterans Benefits Administration (20A5), Department of Veterans Affairs, 810 Vermont Avenue, NW., Washington, DC 20420 (202) 233–3021.

Comments and questions about the items on the list should be directed to VA's OMB Desk Officer, Joseph Lackey, NEOB, room 3002, Washington, DC 20503, (202) 395–7316. Do not send requests for benefits to this address.

DATES: Comments on the information collection should be directed to the OMB Desk Officer within 30 days of this notice.

Dated: November 9, 1993.

By direction of the Secretary.

B. Michael Berger,

Director, Records Management Service.

Extension

1. Request to Lender for Status of Loan Account-LCS, VA Form 26–8778
2. The form is used by VA to obtain pertinent data from the servicer of guaranteed or insured loans and vendee loans sold with VA repurchase agreement on the status of loans in default. The information is used to assure that necessary action is taken to cure the default.
3. Small businesses or organizations.
4. 29,167 hours.
5. 10 minutes.
6. On ocassion.
7. 175,000 respondents.

[FR Doc. 93–28697 Filed 11–22–93; 8:45 am]

BILLING CODE 8320–01–M

federal register

Tuesday
November 23, 1993

Part II

Department of Health and Human Services

Food and Drug Administration

21 CFR Part 820
Medical Devices; Current Good Manufacturing Practice (CGMP) Regulations; Proposed Revisions; Request for Comments; Proposed Rule

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR PART 820

[Docket No. 90N–0172]

Medical Devices; Current Good Manufacturing Practice (CGMP) Regulations; Proposed Revisions; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to revise the current good manufacturing practice (CGMP) regulations for medical devices to: Replace quality assurance program requirements with quality system requirements that include design, purchasing, and servicing controls; clarify recordkeeping requirements for device failure and complaint investigations; clarify requirements for qualifying, verifying, and validating processes and specification changes; and clarify requirements for evaluating quality data and correcting quality problems. In addition, FDA has also, through reorganization and modification of terms, revised the CGMP requirements for medical devices to ensure that they are compatible with specifications for quality systems contained in international quality standards, ISO 9001 "Quality Systems Part 1. Specification for Design/Development, Production, Installation, and Servicing" (Ref. 1), and other applicable international standards, thereby integrating international quality system terminology into proposed CGMP requirements.

DATES: Submit written comments by February 22, 1994. FDA is proposing that any final rule that may issue based upon this proposal become effective 180 days following its publication.

ADDRESSES: Submit written information and comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857. Submit written requests for single copies of this document to the Division of Small Manufacturers Assistance (HFZ–220), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Please provide two self-addressed envelopes to assist the division in processing your requests. All comments and requests should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: William F. Hooten, Center for Devices and Radiological Health (HFZ–300), Food and Drug Administration, 2098 Gaither Rd., Rockville, MD 20850, 301–594–4646.

SUPPLEMENTARY INFORMATION

I. Background

Manufacturers establish and follow quality systems to help ensure that their products consistently meet applicable requirements and specifications. The quality systems for FDA-regulated products (e.g., food, drugs, and devices) are known as CGMP's. CGMP requirements for devices (21 CFR part 820) were first authorized by section 520(f) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360j(f)), which was among the authorities of the Medical Device Amendments of 1976 (Pub. L. 94–295) to the act.

Pursuant to section 520(f) of the act, FDA issued final regulations in the **Federal Register** of July 21, 1978 (43 FR 31508), prescribing CGMP requirements for the methods used in, and the facilities and controls used for, the manufacture, packing, storage, and installation of medical devices. These regulations became effective December 18, 1978, and are codified at part 820. Except for editorial changes to update organizational references in the regulations and revisions to the list of critical devices that was included in the preamble to the final regulations, the device CGMP requirements have not been revised since 1978. This proposed rule is the result of an effort begun in 1990 to revise these regulations.

On November 28, 1990, the Safe Medical Devices Act of 1990 (the SMDA) (Pub. L. 101–629) became law. The SMDA amended section 520(f)(1)(A) of the act to provide clear authority to add preproduction design validation controls to the device CGMP regulations and also added a new section 803 to the act (21 U.S.C. 383) which encourages FDA to work with foreign countries toward mutual recognition of CGMP requirements.

This action is being taken pursuant to those provisions of the SMDA, and in response to notices that appeared in the **Federal Register** of April 25, 1990 (55 FR 17502), and in the **Federal Register** of April 17, 1991 (56 FR 15626), that announced meetings of the agency's Device Good Manufacturing Practice Advisory Committee, at which the need for revisions to the CGMP regulations was explored, and an advance notice of proposed rulemaking (ANPRM) that appeared in the **Federal Register** of June 15, 1990 (55 FR 24544), that announced the agency's intent to revise the CGMP regulations. The agency also announced the availability of a document that appeared in the **Federal Register** of November 30, 1990 (55 FR 49644), entitled "Medical Devices; Current Good Manufacturing Practices (CGMP) Regulations Document; Suggested Changes; Availability," (Ref. 2) (hereinafter referred to as the November 1990 information document) and solicited comments from the public about the document. The agency has met to discuss current good manufacturing practice development with representatives of the European Community (EC), with members of the European Committee for Standardization who have developed the EC's current quality system standards for medical devices, and with representatives of the Canadian Ministry of Health and Welfare and the Japanese Ministry of Health and Welfare. The agency has also participated in numerous industry and professional association seminars and workshops where the proposed revisions of FDA's CGMP regulations were the focus of the meetings.

Thus, FDA's decision to revise the CGMP regulations is based on changes in the law by the SMDA, the agency's discussions with others including its Device Good Manufacturing Practice Advisory Committee, responses to the **Federal Register** notices on this matter, FDA's analysis of recall data, its experience with the regulatory application of the current device CGMP regulations, and its assessment of international quality standards.

II. Summary and Rationale of Proposed Changes

FDA is proposing to add design, purchasing, and servicing controls; modify the critical device requirements; revise certain existing requirements to clarify the intent of the requirements; and harmonize the CGMP regulations for medical devices with quality system specifications in the ISO 9001 International Quality Standard, "Quality Systems Part 1. Specification for Design/Development, Production, Installation, and Servicing" (Ref. 1).

A. Design Controls

Over the last 9 years, FDA has identified lack of design controls as one of the major causes of device recalls (Ref. 3). The intrinsic quality of devices, including their safety and effectiveness, is established during the design phase. Thus, FDA believes that unless

appropriate design controls are observed during preproduction stages of development, a finished device may be neither safe nor effective for its intended use. The SMDA provides FDA with the authority to add preproduction design validation controls to the device CGMP regulations. Based on its experience with administering the CGMP regulations, which currently do not include preproduction design validation controls, the agency is concerned that the current regulations provide less than an appropriate level of assurance that devices will be safe and effective. Therefore, FDA is proposing to add general requirements for design controls to the device CGMP regulations for all class III and II devices and several class I devices.

i. Congressional Hearings

As early as 1984, Congress began holding hearings on medical device failures and FDA's apparent inability to anticipate or address problems within the industry under the 1976 amendments. These hearings focused on deaths resulting from the use of cardiac pacemaker leads which had malfunctioned due to design problems. (See the March 13, 1984, hearing of the House of Representatives' Committee on Energy and Commerce's Subcommittee on Oversight and Investigations.)

As a result of a commitment made by FDA to congressional oversight committees, work began on a document intended to assist medical device manufacturers in planning and implementing a preproduction quality assurance program. In the **Federal Register** of May 19, 1987 (52 FR 18747), the agency published a notice of availability of a draft document entitled "Preproduction Quality Assurance Planning; Recommendations for Medical Device Manufacturers" (Ref. 4). That document was reviewed by the Device Good Manufacturing Practices Advisory Committee and discussed at an open committee meeting held on May 4 and 5, 1988 (Transcript Docket No. 88D–0087). The agency published a notice in the **Federal Register** of October 5, 1989 (54 FR 41165), announcing the availability of the final version of the document.

ii. FDA evaluations

In January 1990, FDA published the results of an evaluation of device recalls that occurred from October 1983 through September 1989, in a report entitled "Device Recalls: A Study of Quality Problems" (Ref. 3). (See 55 FR 21108, May 22, 1990, where FDA announced the availability of the report.) FDA found that approximately 44 percent of the quality problems that had led to voluntary recall actions during this 6-year period were attributable to errors or deficiencies that had been designed into the particular devices and that may have been prevented by adequate design controls. FDA believes that this figure is unacceptable from a public health standpoint. Some of the more egregious examples that FDA found during its evaluation included: (1) The failure to properly identify and establish adequate physical and performance requirements for the device before production; (2) the failure to verify that the device met physical and performance requirements before production; (3) the failure to ensure that device components functioned properly in conjunction with other components; (4) the failure to ensure that the environment would not adversely affect components; and (5) the failure to select adequate packaging materials. These design-related defects involved both noncritical devices (e.g., patient chair lifts, in vitro diagnostics, and administration sets) and critical devices (e.g., pacemakers and ventilators). With respect to software used to operate medical devices, the data are even more alarming. A study of software-related recalls for the period FY 1983—FY 1991 indicated that over 90 percent of all software-related device failures was due to design-related errors, generally, the failure to validate software prior to routine production (Ref. 5).

iii. The Inspector General's Report

In 1990, the Department of Health and Human Services' Inspector General (IG) conducted a study entitled "FDA Medical Device Regulation From Premarket Review to Recall" (Ref. 6). The purposes of the study were to describe FDA's regulatory process for selected medical devices that had been recalled and to identify potential vulnerabilities and strengths in the FDA regulatory system for medical devices. The devices selected for the study were defibrillator/cardiac monitors, balloon catheters, spinal fixation systems, heart valves, lithotripters, balloon inflation devices, insulin infusion pumps, and ventilators. As a result of the study, the IG recommended that FDA incorporate the preproduction quality assurance recommendations into the CGMP regulations for medical devices. Indeed, one company official interviewed as part of this study recommended that preproduction quality assurance requirements be incorporated into the device CGMP regulations.

iv. Proposed Changes

As stated in proposed § 820.1, the purpose of the device CGMP regulations is to help ensure that all devices will be safe and effective and otherwise in compliance with the act. FDA believes that, except for the most simple devices, i.e., certain class I devices, there cannot be an adequate assurance of safety and effectiveness unless proper physical and performance parameters are established during the design stage; such assurance cannot be provided solely by manufacturing controls. Therefore, FDA has concluded that it is essential that those firms and individuals who design class II, class III, and certain class I medical devices discussed in more detail below do so under formal controls that will ensure that, for each intended use of a device, specifications are established and validated to be adequate and that the final design actually meets these validated specifications.

In response to the ANPRM and the November 1990 information document, both of which discussed the proposed addition of design controls, both large and small medical device manufacturers expressed support for the addition of design controls to the device CGMP regulations. For example, one multinational manufacturer of medical devices, pharmaceuticals, biologics, and veterinary medicines (Ref. 7) stated: "The inclusion of design validation in the revised Good Manufacturing Practices (GMP) regulation is a good idea which is being implemented by many device manufacturers. The degree of formally documented validation procedures varies considerably within the device industry." The president of a small manufacturer (Ref. 8) of noncritical devices with 2 years of experience in implementing the specifications for quality systems contained in ISO 9001 said:

> Our experience validates the comments expressed in the summary of the proposed rules: although the implementation can be time consuming, it is our opinion that the medical device product leaving the design phase is in fact of far higher quality than a product without the protocol. By identifying problems early in the design phase, a great deal of subsequent engineering change to an item in production is eliminated. This is probably a net saving to the manufacturer; if the protocol is followed, the development may actually be more efficient. In addition, use of ISO 9001 better equips U.S. manufacturers to compete in a world market.

Thus, in accordance with the SMDA, the agency's experiences with design-related recalls, and comments on the ANPRM and November 1990 information document, FDA is proposing to require the manufacturers

of class II, class III, and certain class I medical devices to establish and implement design controls, with the extent of the controls based on the intended use of the device. FDA welcomes comment on this proposal.

FDA is not proposing to subject the majority of class I devices to design controls because FDA does not believe that such controls are necessary to ensure that such devices are safe and effective and otherwise in compliance with the act. For most class I devices, FDA believes that the production controls in this proposed regulation and the other general controls of the act will be sufficient, as they have been in the past, to ensure safety and effectiveness. However, FDA believes that certain class I devices do raise design-related safety and effectiveness concerns. For such class I devices, the safety, effectiveness, or both, of these devices will, FDA believes, be significantly enhanced by design controls. These devices are identified in the list below. (The list indicates the classification regulation section in title 21 of the Code of Federal Regulations under which the device is listed and the generic name of the device.)

LIST OF CLASS I DEVICES SUBJECT TO CGMP DESIGN CONTROLS

21 CFR	Device
862.2050 through 862.2920.	Instruments, Clinical Laboratory.
868.6810	Catheter, Tracheobronchial Suction.
878.4460	Glove, Surgeon's.
880.4680	Apparatus, Single Patient, Portable Suction.
880.5510	Lift, Patient, Non-AC-Powered.
880.6760	Restraint, Protective.
892.1100	Camera, Scintillation (gamma).
892.1110	Camera, Positron.
892.1130	Counter, Whole Body, Nuclear.
892.1300	Scanner, Rectilinear, Nuclear.
892.1320	Probe, Uptake, Nuclear.
892.1330	Scanner, Whole Body, Nuclear.
892.1410	Synchronizer, Electrocardiograph Nuclear.
892.1970	Synchronizer, Radiographic ECG/Respirator.
892.5650	System, Applicator, Radionuclide Manual.
892.5740	Source, Radionuclide Teletherapy.

When reviewing the list of class I devices to determine whether design controls were needed to ensure the safety and effectiveness of class I devices, FDA concluded that there were two categories of class I devices that should be subject to design controls. The first of these categories consists of devices whose performance cannot be validated properly unless the design process is controlled from the outset. The second category consists of devices that have had design-related problems that have, or could have, significantly affected their safety or effectiveness and injured the user or consumer. This, FDA believes, is a clear signal that design controls are needed. (Some of the devices on the list, such as the radiological devices, fall into both categories.)

Clinical laboratory instruments, cameras, and radiological devices fall into the first category of devices. For these devices, FDA believes that design controls are necessary to ensure that performance specifications are properly established and validated as adequate prior to production. In many cases, these are computerized devices, and thus, FDA believes, proper performance can only be ensured through proper assessment of the design as it is developed during the design phase.

The remaining devices (and the radiological devices as well) fall into the second category. With regard to the suction catheter and the suction apparatus, FDA believes that design controls are necessary to ensure the strength and compatibility of materials and bonded surfaces to minimize separation of components and breakage during use, both of which have been problems in the past. FDA believes that these issues are crucial to the safety and effectiveness of these devices. Similarly, FDA believes that it is critical that the barrier characteristics of materials used in surgeon's gloves be established and proven prior to production of these gloves. With regard to patient lifts and the radiological devices, FDA believes that the specifications for mechanical load capacity, mechanical stability, and strength of materials must be established and assessed as appropriate for their intended use, prior to production, to ensure safety. For protective restraints, FDA believes that design controls are necessary to ensure proper belt design and user instructions.

B. Purchasing Controls

The quality of purchased product and services is crucial to maintaining the intrinsic safety and effectiveness of a device. Many device failures due to problems with components that result in recall are due to unacceptable components provided by suppliers (Ref. 3). FDA has found during CGMP inspections that the use of unacceptable components is often due to the failure of the manufacturer of the finished device to adequately establish and define requirements for the device's purchased components, including quality requirements. Therefore, FDA believes that the purchasing of components, finished devices, packaging, labeling, and manufacturing materials must be conducted with the same level of planning, control, and verification as internal activities.

The appropriate level of control should be achieved, FDA believes, through a proper mix of supplier and in-house controls. Purchasing contracts, orders, or other purchasing documents must clearly and unambiguously specify the necessary requirements for the product or service ordered. This means, of course, that a manufacturer must establish and validate component requirements prior to purchasing the component. (FDA expects these steps to occur during the preproduction design stage.)

Each manufacturer is also responsible for ensuring that purchased products and services conform to specifications, first, by confirming the supplier's quality system and, second, by continued monitoring of the supplier's quality systems and the quality of the items and services received. Accordingly, FDA also is proposing general requirements for manufacturers to assess the capability of suppliers to provide quality products and services, along with general requirements for ensuring that purchasing documents clearly describe the requirements for the product or service purchased.

C. Servicing Controls

FDA finds, as a result of reviewing service records, that the data resulting from the maintenance and repair of medical devices provide valuable insight into the adequacy of the performance of devices. Thus, FDA believes that service data must be included among the data manufacturers use to evaluate and monitor the adequacy of the device design, the quality system, and the manufacturing process. Accordingly, FDA is proposing to add general requirements for the maintenance of servicing records and for the review of these records by the manufacturer. Servicing controls will apply to servicing conducted or controlled by or for finished device manufacturers (e.g., conducted by a manufacturer, employee, agent, or contractor). Manufacturers must ensure that the performance data obtained as a part of servicing are fed back into the manufacturer's quality system for evaluation as part of the overall device experience data.

D. Changes in Critical Device Requirements

In the June 15, 1990, ANPRM, the agency announced that it was considering whether to combine the critical device requirements with the general requirements and modify the critical device terminology in the device CGMP regulations because of duplication of critical and noncritical device requirements and the difficulty that both FDA and industry sometimes have experienced in identifying critical components and critical operations. As a result of the comments received in response to the June 15, 1990, ANPRM and the November 1990 information document, FDA is now proposing to eliminate the critical component and critical operation terminology contained in the present CGMP requirements for devices, and to meld the duplicative requirements into the general requirements of the revised CGMP regulations for medical devices. The increased emphasis on purchasing controls and on establishing the acceptability of component suppliers, however, ensures that the intent of the present critical component requirement is carried forward into the revised CGMP. The addition of a requirement to validate and document special processes further ensures that the requirements of the present critical operation requirements are retained. Process validation is a requirement of the current CGMP and guidelines were published in 1987 to assist manufacturers in establishing process validation procedures (Ref. 9).

FDA is proposing to retain the distinction between critical and noncritical devices for one regulatory purpose. Traceability will continue to be required only for critical devices, and each manufacturer should refer to the definition of "Critical device" in determining whether the traceability requirements apply to that manufacturer's device. FDA will continue to maintain an illustrative list of critical devices to assist device manufacturers in identifying critical medical devices. A current list may be obtained from FDA's Division of Small Manufacturers Assistance (address above), telephone 1–800–638–2041. Neither the proposed nor the current list is intended to be definitive or exhaustive.

E. Overview of Modifications of Specific Requirements

FDA's experience indicates that some existing CGMP requirements for medical devices should be modified, and others clarified, to accomplish their intended purpose. Such is the case with the failure investigations requirements (§ 820.162) and with requirements for investigating device complaints pertaining to death, injury, or health hazards (§ 820.198). The intent of these provisions is to ensure that firms adequately investigate complaints and device failures in order to identify, correct, and prevent the cause of device defects. The present regulations require firms to maintain records to facilitate these activities and to allow FDA to determine compliance with current complaint investigation requirements (§ 820.198) and medical device reporting (MDR) requirements in part 803 (21 CFR part 803). However, FDA has learned through numerous CGMP inspections and investigations of device failures that firms often do not have adequate written procedures for handling complaint reporting and failure investigations. This lack of written procedures, FDA believes, results in inadequate followup which, in turn, results in device failures that could and should have been prevented. Thus, the agency believes that written procedures are necessary to manage the complaint reporting and failure investigation requirements of the device CGMP regulations and to ensure consistent performance of appropriate activities by the proper individuals.

Regarding measures established to identify and solve quality problems, FDA finds that many are structured to focus upon identifying solutions to apparent problems on the basis of immediate information. Inadequate provisions are made for collecting and correlating all salient information to determine and identify the root cause of, and all factors contributing to, a problem and to evaluate all the implications of that cause. Accordingly, the agency intends to clarify existing § 820.20 to require each manufacturer to establish a written program for evaluating all internal and external quality data for purposes of identifying quality problems that result in device defects and developing and implementing corrective action. These clarifications appear in § 820.100.

Because many changes in device components and manufacturing processes can, and do, alter the characteristics of a device and adversely affect performance and quality characteristics in a way that is not readily detectable by visual inspection or routine testing of a device, a manufacturer must be able to demonstrate (i.e., to validate by documented analysis, challenge testing, and evaluation) that the changes accomplish their purpose and have not adversely affected the safety and effectiveness of the device. FDA's recall data show that defects in devices often are caused by changes that were not properly validated (Ref. 3). Had the manufacturers complied with CGMP's, and done the validation that is necessary to establish that a proposed change does what it is supposed to do, and does it properly (without any effect on safety or effectiveness), the need for these recalls could have been avoided. Accordingly, FDA is proposing to clarify that the CGMP requirements for specifications and process changes, currently found in § 820.100(a)(2) and (b)(3), to mandate that device specification and process changes be validated before implementation and that the results of these activities must be recorded.

F. Harmonization

FDA is proposing to reorganize the structure of the device CGMP regulations and modify some of their language in order to harmonize them with international quality standards. Thus, FDA is proposing to relocate and combine certain requirements to better harmonize the requirements with specifications for quality systems in the ISO 9001 quality standard and to use as much common language as possible to enhance conformance with ISO 9001 terminology.

The EC intends to harmonize all marketing requirements for products and services sold in the EC countries to ensure free trade among these countries. This action will effectively create a huge common market of over 320 million people. Medical devices are one of the product categories for which marketing requirements will be harmonized. Harmonization of device requirements within the EC will be accomplished through the issuance of directives that specify the essential requirements that must be met in order to market devices in the EC. Both horizontal standards, applicable to broad categories of products, and vertical standards, which are product specific, will be used in demonstrating conformity with the requirements of the directives. Harmonized quality systems or good manufacturing practice requirements are among the horizontal standards that will be applicable to medical devices.

Two European Standards, EN46001 "Quality Systems—Medical Devices—Particular Requirements for the Application of EN29001" (Ref. 10) and EN46002 "Quality Systems—Medical Devices—Particular Requirements for the Application of EN29002" (Ref. 11) have been prepared by the Joint European Committee for

Standardization/European Committee for Electro-technical Standardization Coordinating Work Group on Quality Supplements. EN46001 will be applicable to those manufacturers subject to design controls who choose to comply with a total quality system that want to market devices in the EC. EN46002 will be applicable to those manufacturers who choose to comply with a production quality system.

EN46001 consists of ISO 9001 requirements plus supplemental requirements specific to medical devices. The revised CGMP regulations will incorporate the requirements of ISO 9001 plus supplemental requirements specific to medical devices that are found in the present CGMP regulations. FDA is working closely with EC officials to harmonize the supplemental requirements of this proposed revised CGMP regulations with those of EN46001.

At a public meeting held on June 19 and 20, 1990 (55 FR 17502), FDA first discussed the possibility of harmonizing the device CGMP regulations with international quality standards with the agency's Device Good Manufacturing Practice Advisory Committee. Subsequently, at an open meeting of the Device Good Manufacturing Practice Advisory Committee held on May 29, 1991 (56 FR 15626), FDA proposed to facilitate harmonization by adopting verbatim the specifications in the ISO 9001 quality standard and to add supplements as necessary to achieve CGMP regulations appropriate for medical devices. However, FDA did not receive the expected permission to reprint for general distribution to the public either the ISO 9001 document or the ISO companion document containing the definitions of quality terms, ISO 8402 (Ref. 12). Of course, FDA would have to publish the documents in the **Federal Register** in order to propose to adopt them as binding regulations under the Administrative Procedure Act (5 U.S.C. 553). Furthermore, FDA decided, upon further reflection, that much of the language of ISO 9001 would need to be adapted for inclusion in the revised CGMP regulations for medical devices.

Therefore, FDA has determined that the most appropriate approach to developing device CGMP regulations equivalent to the quality system specifications in ISO 9001 is to structure the revised CGMP regulations as closely as possible to ISO 9001 specifications and to use similar terminology where appropriate.

FDA believes that revising the device CGMP regulations so they are comparable to the ISO 9001 specifications for quality systems will, once harmonization is achieved, reduce a source of competitive disadvantage to U.S. manufacturers attempting to market devices in the EC. Harmonization of FDA's device CGMP regulations with the medical device good manufacturing practice rules of the EC, and with comparable device good manufacturing practice rules being developed by Canada and Japan, will minimize the number of quality systems with which the U.S. industry must comply to compete in the international market. Harmonization is intended to increase the likelihood that manufacturers need to develop only one quality system for their primary markets. Also, unless FDA's device CGMP regulations are comparable to the EC's harmonized good manufacturing practice standards, FDA will have difficulty establishing mutual CGMP inspection agreements with other countries.

Finally, by requiring all manufacturers to design and manufacture devices under the controls of a total quality system, FDA believes that the proposed changes in the CGMP regulations will improve the quality of medical devices manufactured in the United States for domestic distribution or exportation as well as devices imported from other countries and, thus, are necessary to ensure that only safe and effective devices are distributed in conformance with the act. Thus, harmonization is not intended to, and should not be viewed as, lowering or lessening CGMP requirements. Rather, harmonization means a general enhancement of CGMP requirements among the world's leading producers of medical devices.

III. The Agency's Tentative Conclusions on the Public Comments

A. Comments on the June 15, 1990, ANPRM

As noted previously, FDA published an ANPRM (55 FR 24544, June 15, 1990) which announced that FDA was considering whether the agency should propose to revise the CGMP regulations for medical devices in part 820. At that time, the agency said that the decision to revise the device CGMP regulations would be based on the information and comments submitted in response to the notice; the recommendations of the Device Good Manufacturing Practice Advisory Committee; analysis of FDA's device recall data; the agency's experience in applying the device CGMP requirements in its regulation of medical devices; and the development of harmonized good manufacturing practice regulations by the EC.

In response to the ANPRM, FDA received 53 comments concerning changes to the device CGMP regulations, including comments from industry associations and from medical device manufacturers representing a broad section of small and large firms that manufacture both critical and noncritical devices ranging from the relatively simple to the extremely complex. The general comments covered a wide variety of concerns, from expressing support for implementing practices that would improve the industry's record for design quality, to expressing opposition to design controls. Comments also discussed the elimination of the critical device requirements, harmonization, and reciprocity.

i. Harmonization

1. Several comments said that Congress did not intend for FDA to ensure that manufacturers are competitive in the world marketplace and questioned FDA's legislative authority to undertake harmonization. It was stated that manufacturers and distributors should be responsible for proving compliance with international quality standards, if they wish to export, without Government intervention.

FDA believes the SMDA addresses an important aspect of the agency's role in encouraging the international harmonization of good manufacturing practices. Section 803(a) of the SMDA specifically directs the agency, in entering into agreements with foreign countries to facilitate commerce in devices, to encourage the mutual recognition of good manufacturing practice regulations under section 520(f) of the act, as well as other regulations and testing protocols as necessary. Further, section 514(a) of the act (21 U.S.C. 360d(a) encourages FDA to consult with internationally recognized standard setting organizations when issuing performance standards. FDA does, therefore, have a specific charge from Congress to promote international harmonization of good manufacturing practices. Such a charge is in addition to the agency's authority generally to strive toward harmonization that is consistent with legal requirements.

In this area, harmonization does much more than promote the competitiveness of U.S. device manufacturers; because ISO 9001 promotes a more comprehensive quality assurance system than FDA's present CGMP requirements, FDA believes that this rulemaking will also mean that safer, more effective medical devices are available in the United States. FDA's primary goal in revising the device

CGMP regulations and harmonizing with ISO 9001 is to strengthen its regulations. Thus, FDA would pursue the proposed changes regardless of the progress of the EC's activity to develop harmonized good manufacturing practice standards. Although harmonization with the EC's efforts in this area is secondary, FDA believes it will have significant competitive advantages for the U.S. medical device industry.

2. Several comments questioned FDA's reliance on recall data and whether the changes prompted by FDA analysis of this data would result in the desired corrections and address the quality problems with medical devices.

FDA's recall data are derived from the investigation and resolution of actual medical device failures. Because the recall data relate to actual device failure, FDA believes the data are appropriate for establishing the causes of device failures. The proposed revision of CGMP requirements will require each manufacturer to establish and implement a total quality system appropriate to the device manufactured. The benefits of such quality systems are well established (Ref. 13), and they have also been attested to by manufacturers who have successfully implemented such systems. (See section II.A. of this document.)

In response to the need to provide an economic impact analysis of the proposed CGMP revision, FDA commissioned an independent contractor, the Eastern Research Group, Inc. (ERG), to conduct the analysis (Ref. 14). The contractor's report also supports the public health need for revising the current rules. ERG analyzed FDA's recall and MDR data, interviewed device manufacturers and consultants, and concluded that, because a substantial portion of design problems result from preventable errors or foreseeable design shortcomings spawned by poor design practices, the proposed regulations will improve design practices for a major portion of the industry and thus eliminate a substantial portion of medical device design problems. ERG estimates that, if the proposed design controls are implemented, up to 73 percent of design-related recalls could be avoided. Based on this assumption, ERG estimates that the proposed CGMP regulations would prevent one-third of the design-related problems, avoiding 53 deaths and 1,257 injuries per year. The medical device industry would gain substantial economic benefits from the proposed changes to the CGMP regulations in three ways: cost savings from fewer recalls, productivity gains from improved designs, and efficiency gains for export-oriented manufacturers, who would now need to comply with only one set of quality standards. ERG has estimated that the savings to industry from avoided design-related recalls could be in the tens of millions of dollars.

3. Other comments noted that FDA should not surrender its inspection activity to other countries and that mutual inspection agreements should be pursued with caution.

Because of FDA's limited resources, FDA welcomes opportunities for establishing inspection agreements with other countries, where inspections by the other countries may augment or replace FDA inspections. However, FDA does not enter into such agreements lightly. The adequacy of the foreign country's inspection force, training programs, reporting, and enforcement are all carefully considered and evaluated before FDA enters into such agreements, and FDA preserves its ability to conduct audits.

4. Several comments suggested that FDA issue a guideline, rather than new regulations, to address the changes, while others opposed extending CGMP requirements to devices that are presently exempt.

Guidelines are not binding legal requirements. FDA's experience with guidelines has shown that many manufacturers do not adopt guidelines because they are not mandatory. FDA believes that the proposed changes must be followed to provide adequate assurance that devices are safe and effective. Because experience shows that voluntary guidelines would not be uniformly followed, FDA believes that the changes in the device CGMP regulations must be mandatory requirements.

As for the scope of the requirements, the proposed revised CGMP requirements will apply, as do the present ones, to manufacturers of finished devices distributed in the United States, unless specifically exempt by regulation. Those manufacturers now exempt from the devices' CGMP regulations would also be exempt from the revised CGMP regulations. Moreover, some CGMP requirements may not be applicable to all device manufacturers. For example, those manufacturers which do not produce serviceable devices or devices requiring installation would not be subject to the proposed CGMP regulations that pertain to such devices. Each manufacturer must develop a quality system that is appropriate for each particular device and its design, manufacture, and production processes. FDA will continue to evaluate the adequacy of each manufacturer's quality system and conformance to the selected system during good manufacturing practice inspections.

5. Several comments objected to the elimination of the two-tier system and critical device list associated with the present device CGMP regulations.

FDA believes that experience has shown the need to apply to medical devices generally some of the requirements currently applicable only to critical devices. As discussed earlier, the critical device list will be retained for traceability purposes. FDA welcomes further comment on this proposal.

6. Several of the comments on the proposed addition of design controls to the device CGMP regulations focused on increased costs to small U.S. manufacturers. Comments also claimed that the addition of design controls will slow the introduction of new products. Some comments noted that design concerns should be addressed during FDA's market clearance processes involving premarket notifications for devices, submitted under section 510(k) of the act (21 U.S.C. 360(k)) (510(k) or premarket notifications) and premarket approval applications (PMA's), submitted under section 515 of the act (21 U.S.C. 360e).

Medical device establishments will incur compliance costs in extending their quality systems to meet the proposed FDA regulation. However, FDA believes there is ample evidence to suggest that the long-term benefits will outweigh the costs. As stated previously, these estimated costs and benefits of design controls are contained in the economic impact analysis commissioned by FDA under contract No. 223–91–8100 (Ref. 14).

Moreover, FDA believes, based on comments submitted in response to the ANPRM, that both large and small manufacturers can realize cost and time savings through the proper establishment and implementation of appropriate design controls. (See section II.A. and comment 2 of this document.) In addition, a May 1991 study by the U.S. General Accounting Office indicates that both large and small manufacturers who developed quality improvement programs realized reduced times to develop new products, as well as reduced product defects (Ref. 13), which should result both in reduced costs and increased customer satisfaction.

FDA recognizes that the device industry consists of manufacturers of devices whose design requirements vary significantly based on the intended use of the device. The proposed regulation

sets out the general design control requirements. Under the proposed regulation, each manufacturer is required to develop a detailed design plan for each device it manufactures if it is a class II, class III, or designated class I device and an operating procedure that implements the plan. Device manufacturers are responsible for ensuring that the design plans and operating procedures establish all controls necessary to ensure the production of a safe and effective device. The type of the design controls established and the precise details of implementation are left for each manufacturer to decide, based on the complexity and intended use of the device. FDA will examine these design plans and operating procedures during inspections to determine whether a manufacturer is complying with the device CGMP regulations.

With respect to FDA's market clearance processes, only about 3 percent of all medical devices are subject to premarket approval, and premarket approval requirements do not address all of the design control elements envisioned for the revised CGMP. Further, design controls are not typically evaluated as part of a 510(k) submission.

Many of the comments which the agency received concerning its intention to consider revising the device CGMP regulations pertained to suggested changes and suggested language that were included in the November 1990 information document. These comments are summarized in the following section and discussed in detail in section IV. of this document.

ii. Comments on the November 1990 Information Document

In November 1990, FDA announced the availability of the November 1990 information document (Ref. 2). This document was developed in response to the recommendation, made by the agency's Device Good Manufacturing Practice Advisory Committee during its June 19 and 20, 1990, committee meeting (55 FR 17502), that FDA collaborate with industry in developing language for proposed revisions to the CGMP regulations. The November 1990 information document contained suggested changes and additions to the device CGMP regulations and was mailed to all registered medical device manufacturers to obtain comment and facilitate discussion of the changes being considered by FDA. In response to the November 1990 information document, FDA received 42 letters containing comments on the suggested changes. Letters were received from 10 industry associations (including 1 Canadian and 1 European industry association), 22 manufacturers (both large and small), 2 consulting firms, 2 associations representing medical device users, and members of the agency's Device Good Manufacturing Practice Advisory Committee.

Most of the comments concerned the proposed addition of design controls to the device CGMP regulations, the proposed adoption of CGMP regulations that conform with ISO 9001 specifications for quality systems, and the proposal to modify the critical device requirements and meld the requirements into the general CGMP requirements. The majority of the comments indicated that industry now supports the conformity of FDA's device CGMP regulations with appropriate specifications of ISO 9001 and the harmonization of FDA's device CGMP regulations with the EC's good manufacturing practice requirements for medical devices, EN46001, which is based on ISO 9001.

Approximately one-third of the letters specifically expressed support for the addition of design controls. Others suggested changes in the language proposed for design controls. However, concerns were expressed about retrospective design requirements, the economic impact of design controls, the availability of design data at the manufacturing facility, and the availability of proprietary or trade secret information.

FDA welcomes comments on the proposal to apply design controls to all class III and class II and certain class I devices and on FDA's proposal to make the revised regulations effective 180 days after the date of publication of the final revised regulations. At that time all manufacturers will be expected to have design controls established and implemented. Design control requirements will not be retroactive, although they will apply to design changes made after the effective date to currently marketed products.

All documents required by the CGMP regulations must be maintained at the manufacturing site or other location that is reasonably accessible to FDA. If reasonably accessible (i.e., capable of being provided during the course of an inspection), design control records may be maintained at a facility other than the manufacturing facility, e.g., the research and development (R&D) facility.

The handling of confidential documents is addressed similarly in the current CGMP regulations in § 820.180 and in the proposed revision of § 820.180. Trade secret information is protected by provisions of 21 CFR part 20, which exempts from public disclosure trade secrets and commercial or financial information that are privileged or confidential. In addition, section 301(j) of the act (21 U.S.C. 331(j)) prohibits the release of trade secret information except as set forth in that provision.

The economic impact of design controls was addressed above in comment 2 of section III.A. of this document and is addressed in detail in the economic impact analysis report (Ref. 14).

Pertinent comments received in response to the November 1990 information document are addressed in section IV. of this document.

IV. Analysis of Revised CGMP Regulation for Medical Devices

Following is a description of the proposed revision of the CGMP regulation for medical devices and response to comments received in response to the June 15, 1990, ANPRM and the November 1990 information document. For each section of the proposed revision, references to the applicable section of the November 1990 information document and the requirements of ISO 9001 that have been incorporated into the proposed CGMP regulation are provided. Many of the comments resulted in changes in the language of the proposed regulation.

A. General Provisions (Subpart A)

i. Scope

The scope of the proposed CGMP regulation is described in proposed § 820.1. It will apply to methods used in, and the facilities and controls used for, the design, purchasing, manufacture, packaging, labeling, storage, installation, and servicing of finished devices intended for human use. This is consistent with the scope of ISO 9001. The regulation would not apply to manufacturers of components which are not manufactured specifically for medical devices. However, device manufacturers must assess the quality systems of their suppliers and otherwise ensure that "off-the-shelf" components meet their specifications under proposed § 820.50.

ii. Definitions

Comments on the November 1990 information document recommended adding a number of terms. Those which were pertinent to the proposed changes were added to proposed § 820.3. Terms presently defined in the CGMP regulation that are omitted from proposed § 820.3 because the proposed revisions render them unnecessary are:

Critical component, critical operation, noncritical device, and quality assurance.

Definitions being added to proposed § 820.3 are: Complaint, design history record, design input, design output, design review, establish, executive management, lot or batch, nonconforming, production, quality, quality policy, quality system, record, reprocessing, servicing, special process, specifications, validation, and verification.

Design review, nonconforming, quality, quality policy, and quality system are definitions taken from, or are modifications of, definitions contained in ISO 8402—"Quality vocabulary" (Ref. 12). The November 1990 information document suggested a modification in the term "quality assurance" to include the entire life cycle of a device. In the proposed CGMP regulation, the term "quality assurance" has been deleted and replaced with "quality system," which applies to the entire life cycle of a device. "Executive management" is defined to make it clear which employees are executive management. "Establish" is terminology from ISO 9001. To avoid confusion concerning what is involved when the proposed regulations require manufacturers to establish something, FDA has defined it to include defining, documenting, and implementing. "Record" is defined to make clear that all documents are records for inspectional and recordkeeping purposes. The remaining definitions are taken from the current FDA CGMP regulations or are modifications of definitions taken from other sources.

FDA is also proposing to modify the existing definitions of a number of terms. The existing definition of "component" in proposed § 820.3(c) is modified to clarify that software, firmware, labeling, and packaging are subject to component controls. The definition of "control number" in proposed § 820.3(d) now includes purchasing to indicate that the history of purchasing is a part of traceability. "Critical device" is defined in proposed § 820.3(e) in terms of serious injury, rather than significant injury, to conform with concepts in other FDA regulations, e.g., the Medical Device Reporting (MDR) regulations in part 803. The definition of "Device Master Record" has been expanded to include purchasing, servicing, and installation records. The definition of "finished device" is clarified in proposed § 820.3(l) to include a device that is intended to be sterile, but that is not yet sterilized. In proposed § 820.3(n), the definition of "manufacturer" is revised to include designers, contract sterilizers, specification developers, and initial distributors of imported devices. Ethylene oxide or other sterilant residues are added to proposed § 820.3(o) definition of "manufacturing material." The term "quality audit" in proposed § 820.3(s) replaces the term "audit" in existing § 820.3(b) and the definition has been revised to harmonize with ISO 8402.

7. Several comments on the November 1990 information document suggested a definition for "quality." The proposed definition of "quality" in proposed § 820.3(r) takes into consideration the comments received and has been modified to emphasize that quality means the totality of safety and performance attributes and characteristics that satisfy fitness-for-use.

8. Other comments addressed the need for a definition of the term "signature" to allow for kinds of electronic or computerized signatures or identification in lieu of a written signature. The agency is currently studying whether to adopt a definition of electronic signatures for all regulated industries that includes electronic or computerized identification, and has issued an ANPRM on this issue (57 FR 32185, July 21, 1992).

iii. Quality system

FDA is proposing to revise § 820.5. This section of the proposed CGMP regulation incorporates ISO 9001 4.2 "Quality system." The term "quality system" is used to define a more comprehensive quality program than presently required on the existing CGMP regulations, taking into account the addition of design, purchasing, and servicing controls to the CGMP regulation. No comments were received on the similar language in the November 1990 information document.

B. Quality System Requirements (Subpart B)

i. Management responsibility

FDA is proposing to revise § 820.20. The proposed requirements revise the current requirements in existing § 820.20 to emphasize executive management's responsibility for ensuring that an adequate quality system is established and implemented. This section incorporates the requirements of ISO 9001 4.1 "Management responsibility."

Suggested language for proposed § 820.20 was included in the November 1990 information document. Comments received are addressed below.

Proposed § 820.20(a) requires each manufacturer's executive management to establish the firm's quality policy and objectives. Suggested language for this proposed section was included in the November 1990 information document. This section incorporates the requirements of ISO 9001 4.1.1 "Quality policy." Proposed § 820.20(a) requires the top or executive management of each manufacturer to ensure that the firm's quality policies and objectives are defined, documented, implemented, maintained, and communicated to all employees whose work or responsibilities may affect quality. Quality policy is defined in proposed § 820.3(v).

Executive management has the ultimate responsibility for ensuring that devices produced and distributed are safe and effective. Moreover, executive management's commitment to the quality system and the communication of that commitment to all employees is crucial to the success of the quality system (Ref. 13). FDA's experience indicates that, without such commitment by management and without continuous reinforcement of this management's commitment, employees over time stop adhering to quality system requirements, and the effectiveness of the program erodes. For example, while FDA's CGMP inspection results reveal that most device manufacturers have documented good manufacturing practice programs, because of a lack of executive management's commitment to the program, or a failure to communicate that commitment to employees in practical terms, these programs sometimes are not followed.

9. Several comments in response to the November 1990 information document stated that it was not appropriate to make the understanding, implementation, and maintenance of a quality policy a regulatory requirement and to make executive management responsible for implementation.

FDA disagrees with these comments. Executive management has the ultimate responsibility for ensuring the quality of all devices distributed. Therefore, it is appropriate for executive management to set the pace by establishing the quality policy and maintaining the company's commitment thereto. A critical feature of any successful quality system is executive management's role in providing leadership to the quality program (Ref. 13). Executive management must lead the process, demonstrating a commitment to quality through their daily actions and working to build quality values throughout the organization. FDA believes that through training and continuous reinforcement of the importance of the quality policy

by executive management, employees' understanding of the quality policy can be achieved.

The proposed amendment to § 820.20(b) clarifies that the responsibility and authority for the quality system must be defined and documented and provides examples of quality system activities for which responsibility and authority must be established. This section also establishes general verification requirements and a requirement that manufacturers appoint a management representative with authority over and responsibility for the quality system.Suggested language for this section was contained in the November 1990 information document but has been revised. Therefore, many of the comments no longer apply to the language now proposed for the section. This section of the proposed CGMP regulation incorporates ISO 9001 4.1.2 "Organization."

10. Several comments on similar language that was included in the November 1990 information document complained that the requirement (in proposed § 820.20(b)(3)) for a single individual to manage the quality system at the management level would be too restrictive.

FDA disagrees with these comments. FDA believes it is imperative that one management representative with overall authority be assigned responsibility for the quality system and have access to all parts of the quality system. Responsibility and authority must be established at the top management level to ensure that quality problems are resolved by a person with the ability and authority to implement and oversee a quality control system.

11. One comment asked if the management representative can also be responsible for other activities.

The management representative may carry out the proposed responsibility, either separately or in conjunction with other functions and responsibilities, as long as management effectiveness is not diminished and there is no conflict of interest.

Proposed § 820.20(c) requires each firm to assign a management representative with executive authority to periodically review the quality system to ensure its continuing suitability and effectiveness. An important part of this review is the review of the quality audit results. However, management review responsibilities extend beyond review of audit results and include all aspects of the quality system.

Proposed language for this section was not included in the November 1990 information document. This section incorporates the requirements of ISO 9001 4.1.3 "Management review."

ii. Quality audit

FDA is proposing to retain in proposed § 820.22 the current CGMP requirements of § 820.20(b), but it is proposing to change the title of this section from "Audit procedures" to "Quality audit" to be consistent with ISO 9001 and better identify the function. The term "quality assurance program" is replaced with "quality system" wherever it appears. Also this section states that reports written to document the audit of suppliers and contractors are subject to FDA review and copying. FDA needs access to these reports to determine compliance with proposed § 820.50. Proposed § 820.22 contains the requirements of ISO 9001 4.17 "Internal quality audits."

iii. Personnel

FDA is proposing to redesignate the requirements of CGMP § 820.25(b) to proposed § 820.70(d) because the health condition and hygiene of employees are most pertinent to the production process.

The general requirements of existing § 820.25 on personnel and the current requirements of existing § 820.25(a) on personnel training are being incorporated into proposed § 820.25. FDA notes that training must be more than just an administrative activity. A quality system is no more effective than the people who manage and conduct the quality system activities. Therefore, training must be continuous and appropriate for each employee's current job function.

Since the proposed requirements of this section are existing CGMP requirements, the suggested language for proposed § 820.25 was not included in the November 1990 information document. Proposed § 820.25 incorporates the requirements of ISO 9001 4.18 "Training."

In addition, FDA is proposing a new requirement relating to consultants. Over the years, FDA has observed that a surprising number of firms hire consultants who have no particular expertise in the area in which the firm is seeking assistance. Proposed § 820.25(c) addresses this problem by ensuring that a consultant's fitness for the specific tasks for which he or she is retained is considered and documented.

C. Design Controls (Subpart C)

To implement the design validation provisions of the SMDA, FDA is proposing, in proposed § 820.30, to adopt, as much as practical, the language of ISO 9001 4.4 "Design control." Suggested language for this section was included in the November 1990 information document. As discussed previously in more detail and as set forth in proposed § 820.30, FDA is proposing to apply design controls to all class III and class II devices and certain class I devices.

The quality of a device is strongly influenced by decisions made during the design process. Design deficiencies will affect all devices produced and are progressively more expensive to correct as development proceeds (Ref. 4). Therefore, from both cost and safety standpoints, FDA believes it is essential that a disciplined design program be followed that will minimize the possibility of error and allow design deficiencies to be detected and corrected as early as possible.

To satisfy the proposed design control requirements, each manufacturer will be required to establish a formal, documented program to ensure that design requirements are properly established, verified, and translated into design specifications, and that the design released to production meets the approved design specifications.

12. Two comments on this section said that "Preproduction quality assurance" should be changed to "Design control," as used in ISO 9001.

FDA has retitled the section "Design Controls" and has rewritten the requirements to more closely align them with the specifications of ISO 9001.

The language contained in the information document for proposed § 820.30 has been simplified and incorporates the requirements of ISO 9001 4.4.1 "General."

13. Several comments received in response to the November 1990 information document expressed concern that the costs of implementing design validation would place small manufacturers at a competitive disadvantage.

FDA believes that manufacturers of all sizes benefit from adequate design controls. Under section III.A. and comment 2 of this document, the agency discusses the reduced costs, time savings, international compliance, and other benefits derivable from design controls. An analysis of the cost of implementing design controls for large and small manufacturers is also provided in the report entitled "Economic Analysis of Proposed Revisions to the Good Manufacturing Practices Regulation for Medical Devices" (Ref. 14).

14. Several comments expressed concern that FDA would not have the ability to separate the evaluation of the

design process from the actual device design during good manufacturing practice inspections.

During CGMP inspections, the FDA investigator will review each manufacturer's design plan and the program that each manufacturer establishes to satisfy the applicable CGMP regulation design control requirements. The investigator will evaluate both the adequacy of the methods and procedures and each firm's compliance with these methods and procedures. Normally, the investigator will evaluate the process used to establish, evaluate, and release the finished design, rather than evaluate the adequacy of the design. However, if evidence of unsafe or ineffective designs is detected during good manufacturing practice inspections, the FDA investigator has an obligation under the act to investigate.

Proposed § 820.30(b) incorporates the requirements of ISO 9001 4.4.2 "Design and development planning," 4.4.2.1 "Activity assignment," and 4.4.2.2 "Organizational and technical interfaces." Many comments received on this section of the information document no longer apply, because the proposed requirements are a major revision of the suggested language. Pertinent comments are discussed below.

Proposed § 820.30(b) requires each manufacturer to establish a written plan that is appropriate to the design, that defines each design activity, including design verification points and methods, and that identifies the person responsible for each activity. The success of any activity is dependent upon knowing what is to be done. Therefore, the design process and its interface with other internal and external organizational groups must be defined as much as possible before the design process begins. Effective planning includes consideration of production needs, e.g., production environment and equipment, workmanship requirements, process development, and validation.

Proposed § 820.30(b) also requires each manufacturer to assign to designated individuals the responsibility, and provide these individuals with sufficient authority, to carry out the required design control activities. These individuals must be qualified to carry out their assigned activities and must be provided with sufficient and adequate resources to carry out the assigned activities.

In some firms, individuals outside the design unit may participate in the design program. When the design activity involves organizations or groups in addition to the design unit, organizational and technical interface controls must be in place to ensure that needed information and data are transferred in a timely and systematic manner. Determinations that provide the basis for such controls, which should be made during the planning stage, include: What information is to be transmitted; by whom, to whom, and by what means the information is to be transmitted; and what review process is to be followed and what records are to be maintained for the information that is to be transmitted.

Proposed § 820.30(c) has been retitled "Design input" in response to comments. The language provided in the information document for this section has been substantially simplified. Proposed § 820.30(c) requires manufacturers to establish controls to ensure the design requirements are properly established. This section incorporates the language of ISO 9001 4.4 "Design input," and also specifies that the needs of the user must be reflected in the design requirements.

Design input is the design definition phase, or the design requirements definition phase, in which the design's physical and performance features or characteristics are defined. The design input is typically configured in the form of a description of all pertinent design requirements, such as physical, functional, environmental, safety, and regulatory requirements. This phase also includes the identification of components that require development and/or analysis.

FDA notes that the establishment of labeling requirements is an important element of design input. When establishing the design and labeling requirements, a manufacturer must consider a variety of factors, including the safety needs of the users (e.g., operators and patients), the environment in which the device will be used (e.g., in the home, by a health care professional, in an operating suite, in an emergency vehicle), reliability, safeguards against misuse, and, where applicable, maintainability and serviceability. Adequate maintenance instructions must be provided, so that the user can maintain the device's safety and effectiveness. To ensure manufacturability, this phase should also include the establishment of manufacturing requirements. To ensure that conformance to specifications can be determined, this phase should include quality control requirements.

15. Several comments stated that the terms "Safety and effectiveness" should be deleted in favor of "Performance" because current investigational device exemption and PMA regulations adequately address safety and effectiveness. The comments maintained that FDA is prohibited from evaluating safety and effectiveness as part of any CGMP requirement dealing with design controls because the language of section 18 of the SMDA, which added design validation to the provisions of section 520(f)(1)(A) of the act, contained an exclusion that stated "preproduction design validation (including a process to assess the performance * * * but not including an evaluation of the safety or effectiveness of a device.)"

In response to these comments, the terms "safety and effectiveness" have been deleted and replaced with "intended use of the device." However, FDA notes that the CGMP requirements are, after all, intended "to assure that [a] device will be safe and effective and otherwise in compliance with [the act]" (section 520(f)(1)(A) of the act) and that the statutory basis for the CGMP requirements is not restricted to section 520(f) but encompasses other provisions concerned with safety and effectiveness, e.g., section 515 of the act.

Moreover, because issues of safety and effectiveness affect a device's ability to perform its intended use, FDA's focus upon the process used to design and assess device performance does not relieve a manufacturer of the responsibility of establishing and maintaining controls that set and assess the proper level of safety and effectiveness of the design. Manufacturers must establish the level of safety and effectiveness that is commensurate with the intended use of the device and ensure that the design adequately reflects these needs before it is released to production. FDA will evaluate the adequacy of the controls that manufacturers have established to ensure safety and effectiveness during good manufacturing practice inspections.

16. In responding to the November 1990 information document, several comments said that the words "ambiguous" and "incomplete" should be deleted from the language suggested for the design requirement that specified, "All incomplete, ambiguous, or conflicting design requirements should be resolved * * *." These terms have been deleted because FDA determined they added nothing to the requirements. FDA intends that manufacturers should comprehensively document design requirements. In accordance with recognized quality assurance principles, FDA expects

design specifications to be complete, clear, and consistent (Ref. 4).

Proposed § 820.30(d) will require manufacturers to conduct design verification procedures appropriate to the intended use of the device. The suggested language contained in the November 1990 information document for this section has been revised. Verification methods may vary and include, among other things, hazard analysis, failure mode effects analysis, and performance testing. The frequency and extent of the assessments are left for each manufacturer to decide, but should be based on such factors as: The intended use of the finished device, its complexity, the extent of innovation and new technology introduced, and the degree of standardization. Verification must include ensuring the design is adequate for its intended use. This includes, where applicable, software validation and hazard analysis. Each manufacturer should establish a design process hierarchy and assess the acceptability of the design, both during the stages of design development and before the design is released to production. A design review should be performed at the conclusion of each stage to evaluate the design requirements and the capability of the design to meet the design requirements and to identify problems and propose solutions.

Proposed § 820.30(f) requires manufacturers to document the design output and ensure the output meets approved design requirements. Proposed § 820.30(f) was included in the November 1990 information document. The proposed requirement incorporates the requirements of ISO 9001 4.4.4 "Design output." Design output occurs at various phases in the design process, and the proposed design output requirements are intended to apply to all phases of the design process. The final design output is the product of the design process and typically consists of the final component, manufacturing material, and device specifications and drawings as well as all instructions, software, and procedures that are used for purchasing, production, installation, maintenance, and servicing. These documents are included in the device master record.

Proposed 820.30(g) is a supplement to ISO 9001 requirements. Under proposed § 820.30(d)(3), before devices are released for routine distribution, finished devices must be sampled from the first three production runs and tested for performance under actual conditions of use or simulated use conditions in the environment or simulated environment in which the device is expected to be used. FDA considers this a critical element of the validation of the manufacturing process. The requirement to conduct simulated use testing of finished devices is presently found in § 820.160 of the CGMP regulation as part of finished device inspections and is being moved to proposed § 820.30(d)(3) because FDA believes that simulated use testing at this point is more effective in ensuring that only safe and effective devices are produced. Manufacturers must also conduct such tests when they make changes that could affect safety or effectiveness in the device design or the manufacturing processes. The extent of the testing conducted should be governed by the risk(s) the device will present if it fails. FDA considers these procedures essential for ensuring that the manufacturing process does not adversely affect the device (Ref. 9).

Manufacturers may not use prototypes developed in the laboratory or machine shop as test units to meet these requirements. Prototypes may differ from the finished production devices. During research and development, conditions are typically better controlled and personnel more knowledgeable about what needs to be done and how to do it than are regular production personnel. When going from laboratory to scaled-up production, standards, methods, and procedures may not be properly transferred or additional manufacturing processes may be added. Often, changes not reflected in the prototype are made in the product to facilitate the manufacturing process. Proper testing of devices that are produced using the same methods and procedures as those to be used in routine production will prevent the distribution and subsequent recall of many unacceptable medical devices.

17. One comment said that the phrase "before releasing a design to production" in the November 1990 information document under "Design verification" should be deleted. This phrase has been deleted in proposed § 820.30(d) in response to the comment and replaced with the language in proposed § 820.30(g).

18. Several comments objected to use of the term "worst-case conditions" in the November 1990 information document. The term has been deleted in response to the comments.

19. One comment stated that the design verification wording implies that no production can take place until every process and piece of equipment is in the final form anticipated for full-scale production. In response, the wording of the proposed requirements for simulated use testing has been changed to require sampling and testing of the first three production runs. However, samples must be taken from devices that were produced using the same specifications, production and quality system methods, procedures and equipment that will be used for routine production.

20. One comment stated that design "requirements" should be changed to design "specifications." In drafting the revisions to the CGMP regulation, FDA has adopted the definitions for specifications contained in the November 1990 information document, ISO 8402 "Quality vocabulary" (Ref. 12). A specification is a document that contains requirements. Requirements thus make up a specification. The design "specifications" contain the "requirements" for the design. In this respect, FDA has deleted use of the term "requirement" in favor of specifications, and has defined "Specifications" in proposed § 820.3(bb).

Proposed 820.30(h) is a supplement to the ISO 9001 requirements. Under proposed § 820.30(h) a designated individual must be responsible for approving the release of the design to production.

The requirements of proposed § 820.30(i) incorporate the requirements of ISO 9001 4.4.6 "Design changes." Proposed § 820.30(i) was included in the November 1990 information document. It requires manufacturers to document changes made to the design specifications during the design phase and ensure that changes are adequate for their intended use.

21. Several comments said that maintaining records of design changes would be unduly burdensome.

FDA recognizes that many design changes are made during the design process, but that not all become part of the final approved design. Manufacturers are not expected to maintain records of all changes proposed during the very early stages of the design process. However, all design changes made after design review that are approved for incorporation into the design, and those changes made to correct design deficiencies, must be documented. The records of these changes create a history of the evolution of the design, which can be invaluable for failure investigation and for facilitating the design of future similar products. Such records can prevent the repetition of errors and the development of unsafe or ineffective designs.

22. Several comments suggested that the reference to clinical evaluations under "Design changes," as contained in the November 1990 information document, was unnecessary and should

be deleted. FDA has deleted the reference to clinical evaluations in response to these comments.

23. One comment recommended that any reference to change should be eliminated and the focus should be on the validation of the final, full-scale, production design. Any changes after that time would require documentation.

FDA disagrees. The safety and effectiveness of devices cannot be proven by final inspection or testing. Product development is inherently an evolutionary process. While change is a healthy and necessary part of product development, quality can be ensured only if change is controlled and documented throughout the development process. Each manufacturer must establish criteria for evaluating changes to ensure that the changes are appropriate for its designs.

Proposed § 820.30(j) requires manufacturers to maintain a record that contains the complete design history of a device. The proposed requirement to maintain a design history record is a new requirement that, although not specified by ISO 9001, is necessary so that manufacturers can exercise control and accountability over the design process and thereby maximize the probability that the final design conforms to the design specifications.

D. Document Controls (Subpart D)

Proposed § 820.40 is a revision and clarification of existing § 820.100. This proposed section was not included in the November 1990 information document. It incorporates the requirements of ISO 9001 4.5 "Document control."

Under proposed § 820.40, all manufacturers must establish document controls to ensure the clear and precise control of all documents that are required by the CGMP regulations. These controls include establishing a formal, documented system that defines how and by whom documents will be produced, reviewed, and approved, and the process to be used for updating documents and defining the responsibility for the distribution and maintenance of all required documents and the removal of obsolete documents.

Proposed § 820.40(a) was not included in the November 1990 information document. This section of the proposed CGMP regulation incorporates the requirements of ISO 9001 4.5.1 "Document approval and issue." It requires manufacturers to designate employees to review and approve all documents prior to distributing them. The 1990 information document suggested modifying current requirements in § 820.100 to better control document issuance and obsolete documents. These controls are set out in proposed § 820.40(b).

24. In response to the November 1990 information document, several comments said that all obsolete documents should not have to be removed, because they may still have use. The agency disagrees. If obsolete documents still have use, they are not obsolete, but may require reidentification.

25. Other comments said that use of the term "practical number" needs interpretation.

After reviewing these comments, FDA believes it is best to delete the term, and will address the issue in future guidelines.

Proposed § 820.40(c), which requires certain controls for specification changes, was not included in the November 1990 information document in its present form. Reference in proposed § 820.40(c) to adequate validation of specification changes was mentioned in the November 1990 information document in addressing the need to qualify and validate specification changes. This section of the proposed CGMP regulation incorporates ISO 9001 4.5.2 "Document changes/modification."

Proposed § 820.40(c) is a clarification of § 820.100(a)(2) and (b)(3). Existing CGMP requirements state that the device design (including components, packaging, and labeling) and all production and quality system specifications and methods must be documented (§ 820.181). All changes to these specifications must also be documented (§ 820.100(a)(2) and (b)(3)). FDA's review of recall data indicates that many recalls occur because of failure to validate specification changes to ensure such changes are adequate for their intended use (Ref. 3). Proposed § 820.40(c) requires manufacturers to validate that changes are adequate for their intended use before implementation.

In addition, to ensure that each manufacturer fulfills its responsibility under 21 CFR 807.81 or 21 CFR 814.39, proposed § 820.40(c) contains a requirement to consider the need to submit a 510(k) or PMA supplement when significant changes are made to device or manufacturing process specifications.

26. Several comments said that requiring all specification changes to be validated, as was proposed in the November 1990 information document, is overly burdensome and unnecessary. The comments added that not all specification changes affect product function.

In response to the comments, the requirement in this proposed section to validate changes is modified to require that all changes that may affect quality must be validated. Quality is defined in proposed § 820.3(r).

E. Purchasing (Subpart E)

FDA is proposing to replace the requirements of § 820.80 with the proposed Subpart E—Purchasing Controls and Subpart H—Inspection and Testing. A similar proposal was included in the November 1990 information document. Subpart E incorporates the requirements of ISO 9001 4.6 "Purchasing."

The failure to implement adequate component controls has resulted in a significant number of recalls due to component failures. Most of these were due to unacceptable components provided by suppliers (Ref. 3). FDA believes that the explicit addition to CGMP requirements of the purchasing controls of ISO 9001 will provide additional assurances that only acceptable components are used.

To ensure that purchased items and services conform to specifications, purchasing must be carried out under adequate controls, including the assessment and selection of suppliers, the clear and unambiguous specification of requirements and the performance of suitable inspection and testing. Each manufacturer must establish an appropriate mix of supplier and incoming controls to ensure that purchased components, finished devices, and manufacturing materials are acceptable for their intended use.

The specifications for the finished device cannot be met unless the individual parts of the finished device meet specifications. The most efficient and least costly approach to ensure that only acceptable components, packaging, and labeling are used is to ensure that only acceptable components, packaging, and labeling are received. This means that only suppliers who can consistently meet specifications should be used. Thus, proposed § 820.50(a), which incorporates ISO 9001 4.6.2 "Assessment of sub-contractors," requires manufacturers to assess the ability of suppliers to provide acceptable components, finished devices, manufacturing materials, and services.

The extent of the assessment, and the type and extent of control exercised by the manufacturer, are dependent upon the significance of the product or service purchased, and, where applicable, upon the previously demonstrated capability and documented performance of the

supplier. Selected suppliers should have a demonstrated capability to provide components, finished devices, manufacturing materials, or services that meet all of the needed requirements. Where it is not practical to assess the capability of suppliers and contractors, manufacturers must ensure the adequacy of supplied and contracted components, finished devices, manufacturing materials, and services through traditional incoming inspection or testing, with the degree of inspection and testing based on the intended use of the product or service.

27. Several comments stated that the assessment of supplier/subcontractor requirements, as set forth in the November 1990 information document, were too detailed. Other comments pointed out that each manufacturer does establish its own detailed criteria for supplier selection and should be left to do so on its own. FDA has reviewed the comments and has reduced the detail contained in the November 1990 information document.

Another comment suggested that quality is not the only consideration when selecting a supplier. Although FDA agrees that quality is not the only consideration when selecting suppliers, it is nevertheless a crucial consideration and may not be disregarded.

Proposed § 820.50(b) incorporates the requirements of ISO 9001 4.6.3 "Purchasing data" and specifies that controls must be established to ensure that specifications are properly described in the purchasing documentation. Often, purchased components do not meet the required specifications because the specifications provided to the supplier are unclear or incomplete. Ensuring that purchased components, finished devices, packaging, labeling, manufacturing materials, and services meet specifications begins with a clear definition of requirements. The proposed regulation specifies that controls must be established to ensure that specifications are properly described in the purchase or contract documentation.

28. Several comments, in response to the November 1990 information document, referred to the need for flexibility in requiring that purchasing documents contain "data clearly describing the item or service ordered."

In response to the comments, FDA has revised this proposed requirement. The proposed requirement now specifies that the purchasing documents shall describe or, when appropriate, reference published standards or specifications for the item or service purchased.

29. Several comments expressed concern that mandating that a designated individual review and approve purchasing documents was overly restrictive and did not allow for computerized checking.

In response to the comments, the requirement has been revised and no longer includes a reference to a designated individual. Nevertheless, because accountability is crucial, the signature of the person responsible for approving a purchasing document must be recorded.

F. Identification and Traceability (Subpart F)

i. Identification and traceability

Proposed § 820.60 imposes general controls to ensure that components, finished devices, and manufacturing materials are properly identified until they leave the manufacturer's control, but does not mandate traceability for noncritical devices. However, when a noncritical device manufacturer decides to establish traceability, traceability must be established using current, acceptable practices, i.e., identification such as serial or control numbers must be assigned.

The requirements in proposed § 820.60 were included in the November 1990 information document and incorporate the general requirements of ISO 9001 4.8 "Product identification and traceability."

30. Several comments, in response to the November 1990 information document, said that traceability should be limited to critical devices. While FDA was not suggesting that traceability was required for noncritical devices, the point has been clarified by placing traceability requirements for critical devices under a separate section in proposed § 820.65.

ii. Critical devices, traceability

Proposed § 820.65 retains traceability requirements for critical devices and is a supplement to ISO 9001.

31. Several comments agreed that the elimination of "critical component" was overdue, but claimed that not every component requires traceability even in a critical device.

FDA does not agree with these comments. Where traceability of components is important to prevent the distribution of nonconforming critical devices, critical device manufacturers must maintain traceability of components to a level that will enable the identification of the quality status of specific lots and batches of components, so that a problem component, or potential problem components, can be identified and traced to the supplier.

While FDA understands that traceability entails additional cost, it reminds manufacturers that, if a product recall is necessary, more devices would be subject to recall if lots of specific devices are not traceable, with associated higher recall costs to the manufacturer.

G. Production and Process Controls (Subpart G)

i. Process control

Subpart G—Production and Process Controls identifies the production conditions and controls that must be addressed when manufacturing medical devices. All are existing CGMP requirements, interpretation of CGMP's, or revisions of existing CGMP requirements, some of which are relocated from other parts of the CGMP regulation.

Proposed § 820.70(a) will require manufacturers to establish and implement sufficient and adequate process controls to ensure that the finished devices meet specifications. This is currently a requirement in § 820.100. No changes were suggested in the November 1990 information document for this proposed section; therefore, no comments were received. This section incorporates ISO 9001 4.9.1 "General." Written production methods, procedures, and workmanship criteria are required where deviations from device specifications could occur as a result of the absence of these production process controls. The proposed requirements are a clarification of the existing requirements in § 820.100(b).

Proposed § 820.70(b) duplicates existing § 820.46, except that static electricity is added to the list of conditions which may require control. Existing § 820.46 is redesignated as proposed § 820.70(b) because these requirements are pertinent to the production process. Because these proposed requirements are existing CGMP requirements, they were not included in the November 1990 information document and no comments were received. The requirements of this section of the proposed CGMP regulation are not contained in ISO 9001 and are a supplement to ISO 9001 4.9 "Process control."

Proposed § 820.70(c) is a combination of existing §§ 820.25(b) and 820.56. These requirements are redesignated as § 820.70(c) because they are pertinent to the production process. This proposed section was not included in the November 1990 information document and, therefore, no comments were received. Proposed § 820.70 (d), (e), and

(f) are existing CGMP requirements. The requirements of this section of the proposed CGMP regulation are not contained in ISO 9001 and are a supplement to ISO 9001 4.9 "Process control."

The proposed requirements in § 820.70(g) duplicate existing requirements in existing § 820.60, with some minor additions. For example, the phrase "adequate for its intended use" and the word "use," which are not contained in the language of existing § 820.60, are used in proposed § 820.70(g) to clarify that manufacturing equipment must be "adequate for its intended use," and to clarify that the equipment must be appropriately designed to facilitate not only maintenance, adjustment, and cleaning, but also use.

The proposed requirement in § 820.70(g), that manufacturing equipment must be adequate for its intended use, was included in the November 1990 information document. There were no comments on the suggested revision. The other proposed changes were not included in the information document. The requirements of this section of the proposed CGMP regulation are not contained in ISO 9001 and are a supplement to ISO 9001 4.9 "Process control."

Proposed § 820.70(h) is a combination of the CGMP requirements for automated operations contained in existing §§ 820.61 and 820.195. Such operations must be evaluated, and when necessary, the software validated according to formal protocols. The language of this section was included in the November 1990 information document. It was also cited as substitute language for existing requirements in that document which proposed deleting existing requirements to validate automated systems in § 820.61 and § 820.195. The requirements of this section are a supplement to ISO 9001.

32. Comments which addressed proposed requirements to validate automated systems stated that not all software requires validation; for some software, inspection and testing are alternatives.

FDA disagrees. Inspection and testing are not alternatives to validation; they are means to accomplish validation. Thus, inspection and testing may, in some cases, be appropriate to ensure that software is acceptable for its intended use in a production process. Such inspection and testing should be documented in a written protocol; this may accomplish validation. However, all software used in production must be reviewed for adequacy and properly validated before use.

ii. Special processes

FDA added proposed § 820.75 which provides requirements for special processes to clarify that process validation is required for many processes and is a CGMP requirement. A "Special process" is defined in proposed § 820.3(aa). Because the results of special processes cannot be verified by inspecting or testing the process results, special processes must be validated and carefully monitored during processing to ensure they will consistently produce the desired results.

Although proposed § 820.75 was not included in the November 1990 information document, process validation was discussed as a CGMP requirement in that document. The November 1990 information document did not use the term "special processes," as is done in proposed § 820.75, but otherwise described such a process. Many manufacturers have expressed confusion as to which processes should be validated in a given manufacturing process. FDA believes the clarification of validation requirements in proposed § 820.75, in conjunction with the definition of "Special process" in proposed § 820.3(aa), will assist manufacturers in deciding which processes to validate. This section incorporates the requirements of ISO 9001 4.9.2 "Special processes."

H. Inspection and Testing (Subpart H)

i. Inspection and testing

The requirements proposed in § 820.80 were not included in their present form in the November 1990 information document because they are primarily existing CGMP requirements. These requirements incorporate the provisions of ISO 9001 4.10 "Inspection and testing" and are incorporated in existing §§ 820.20(a)(4) and 820.80.

Proposed § 820.80(a) will require manufacturers to formalize assessment methods and procedures and ensure that they are adequate for their intended use and performed correctly. During production there are typically three phases where inspection, testing, or verification should take place: When receiving raw materials or components; during the manufacturing process; and prior to release of the finished devices. It is important that each of these activities be controlled and the results recorded in quantitative data to provide objective evidence of the completion of the operation. Manufacturers must use a combination of in-house inspection and testing methods, validation, and process control, to ensure conformance to design and process specifications. Proposed § 820.80(b) contains basically the same requirements as existing § 820.80(a). This section of the proposed CGMP regulation incorporates ISO 9001 4.10.1 "Receiving inspection and testing."

Each manufacturer must establish an appropriate mix of supplier and incoming controls to ensure that purchased components, finished devices, packaging, labeling, and manufacturing materials are acceptable for their intended use. The proposed language for this requirement will provide manufacturers some flexibility in deciding whether to carry out acceptance procedures at the supplier, under contract, or in-house, or some combination of these approaches.

The requirements in proposed § 820.80(c) are now contained in existing §§ 820.20(a)(2) and, 820.100 and therefore were not proposed in the information document. They incorporate the provisions of ISO 9001 4.10.2 "In-process inspection and testing." Proposed § 820.80(c) requires manufacturers to conduct in-process inspections and tests according to written procedures and to record the results, when the manufacturing process could affect the product's quality. The results must be recorded and maintained in the device history record.

Proposed § 820.80(d) is essentially identical to § 820.160, except that the requirement for actual or simulated use testing is being moved to proposed § 820.30(g), and the requirement that addresses sampling plans is moved to proposed § 820.250. These requirements were not included in the November 1990 information document. FDA believes the requirement for simulated use testing set out in proposed § 820.30(g) will be more effective at the end of the design process and following changes to the device and process. A new requirement is added to ensure that all acceptance data are present and reviewed before finished devices are released for distribution. This is a clarification of the requirement in § 820.20(a)(1). Final inspections and tests alone are not sufficient to ensure that devices are manufactured according to the requirements of the device master record. Objective evidence must be provided and reviewed before devices are distributed.

FDA proposes to remove existing § 820.161 because these requirements are now incorporated under proposed §§ 820.90, 820.100, and 820.80(d).

A proposal that existing § 820.161 be relocated was included in the November

1990 information document. No comments specific to that proposal were received, other than the general comments on elimination of the critical device requirements. (See section III.A. of this document.) The requirements of proposed § 820.80(d) incorporate ISO 9001 4.10.3 "Final inspection and testing."

Proposed § 820.80(e) clarifies that all inspection and test results must be recorded in the device history record and incorporates ISO 9001 4.10.4 "Inspection test records." This proposal was not included in the information document. It is consistent with existing § 820.184.

ii. Inspection and test equipment

Proposed § 820.84 consists of existing § 820.61, except that proposed § 820.84 (d) and (e) are added to ensure that, once calibrated, the integrity of the equipment calibration is maintained. This section incorporates ISO 9001 4.11 "Inspection, measuring, and test equipment."

The current requirement contained in § 820.61 to validate all automated production and quality assurance systems is being redesignated as proposed § 820.70(h), which contains a general validation requirement for all automated processes. Reference to removing and redesignating validation requirements for automated systems was made in the November 1990 information document. Comments on this point are addressed in section IV.G. of this document which discusses proposed § 820.70(h).

iii. Inspection and test status

Proposed § 820.86 incorporates ISO 9001 4.12 "Inspection and test status" and requires manufacturers to identify the inspection and test status of all components, finished devices, and manufacturing materials at all phases of purchasing and production. This proposed section was not included in the November 1990 information document. It must be possible to quickly and clearly establish the inspection status at any phase of purchasing and production and, in particular, identify those items which do not conform to specifications. This requirement is already a CGMP requirement contained in existing §§ 820.80 and 820.100.

I. Nonconforming Components and Devices (Subpart I)

Proposed § 820.90 is a revision of existing §§ 820.115 and 820.116 and sets forth the requirements for nonconforming components and devices. Similar proposed requirements were included in the November 1990 information document. Proposed § 820.90 incorporates the requirements of ISO 9001 4.13 "Control of nonconforming product."

Each manufacturer's quality system must include controls that will ensure that components, finished devices, or manufacturing materials that do not conform to specifications are not inadvertently used or distributed. This section is applicable to manufactured as well as purchased components, finished devices, or manufacturing materials and returned finished devices.

Purchasing and manufacturing processes sometimes yield suspect or defective items. In order to ensure that only acceptable finished devices are distributed, manufacturers need methods for preventing further processing, distribution, or installation of nonconforming components, finished devices, and manufacturing materials. The method of identifying and determining the disposition of nonconforming components, finished devices, and manufacturing materials will vary, depending upon the type of device produced. In all cases, the methods and procedures used to identify and control nonconformance must be documented and included in the device master record. The investigation of nonconforming items is an important part of the quality system. The results of the investigation of nonconformance provide valuable information that may be used to prevent reoccurrence of nonconforming components and devices. This activity, if properly designed, can also result in cost savings to the manufacturer and increased customer satisfaction.

33. With respect to the investigation of nonconforming components and finished devices, several comments stated that an investigation is not always necessary when a nonconforming product is identified.

FDA disagrees. Unless the defect is solely cosmetic (e.g., paint or polishing defects), manufacturers must investigate and establish both the cause and effect of the defect or nonconformance. If the cause and effect of nonconformance is already suspected, then the documented investigation need only confirm the cause and effect. When cause and effect are unknown, documented investigation must be conducted to the level necessary to determine the cause of nonconformance and the effect on quality.

34. One comment said that there are numerous types of repair and rework activities that take seconds to perform but would take hours to write up.

FDA believes the proposed good manufacturing practices accommodate this comment. The recordkeeping requirement is intended to ensure that nonconforming components and finished devices are identified and not distributed until they meet specifications. Each manufacturer must develop recordkeeping sufficient to achieve this requirement that is appropriate to the activity.

35. One comment asked if this section applied to the release of nonconforming materials without repair, rework, or reprocessing. When this disposition is chosen, the manufacturer must evaluate and document the decision and ensure that it does not compromise the finished device safety and effectiveness.

J. Corrective Action (Subpart J)

The regulations set forth in this proposed subpart incorporate the specifications contained in ISO 9001 4.14 "Correction Action," which are implicit in existing § 820.20(a)(3) and (a)(4). The ISO requirements are modified in proposed subpart J to clarify that corrective action activities must be documented and to create order in the approach to problem detection and resolution. Because proposed § 820.100 incorporates the current requirements under § 820.162, existing § 820.162 is being removed from the revised CGMP regulations.

Proposed § 820.100 requires manufacturers to establish a program for the collection, correlation, and evaluation of internal and external quality data for the purpose of detecting and preventing quality problems. A manufacturer is also required to develop solutions to any problems found, to identify, implement, verify, and document corrective action. These proposed requirements were included in the November 1990 information document under the organization section. Trend analysis was suggested in the information document as a means of evaluating data.

Proposed § 820.100(a)(1) through (a)(5) require that each manufacturer's quality system must include a documented, systematic method for identifying and eliminating the causes of nonconforming components, finished devices, and manufacturing materials. Under proposed § 820.100(a)(6), relevant quality information must be regularly reported to and monitored by management. Management must compare the information with quality objectives and identify opportunities for improvement in design, manufacturing, and the quality system.

36. Several comments objected to the specification of just one method (trend analysis) as a quality assurance tool. In proposed § 820.100(a)(1), the

requirement to evaluate data for nonconforming products is rewritten to align with ISO 9001 and to specify that trend analysis is to be conducted. The proposed requirement specifies that manufacturers must analyze all quality data, including complaint files and service reports, to detect systematic problems that cause nonconformance and other quality problems. Trend analysis is not a single analytical method. Rather, trend analysis requires a manufacturer to use an appropriate statistical methodology to determine whether systemic or unanticipated problems are occurring with a product or whether problems are occurring at a greater than anticipated frequency. Trend analysis is the appropriate method for conducting this analysis.

K. Handling, Storage, Distribution, and Installation (Subpart K)

i. Handling

The requirements of proposed § 820.120 are a revision of existing § 820.40. This proposed section incorporates ISO 9001 4.15.2 "Handling," and was not included in the November 1990 information document.

Each manufacturer must establish, as part of the quality system, documented controls that will ensure that the activities involved in the handling, moving, and holding of components, finished devices, and manufacturing materials will have no adverse effects on these items. Controls shall include provisions for preventing mixups.

ii. Storage

Proposed § 820.122 is a combination and revision of the current storage requirements in §§ 820.80(b), 820.40, and 820.150. This section incorporates ISO 9001 4.15.3 "Storage" and was not included in the November 1990 information document. Proposed § 802.122 specifies that the quality system must include controls for all storage areas that are adequate to ensure that the quality of components, finished devices, and manufacturing materials are not adversely affected during devices storage and that all deteriorated or rejected and nonconforming items are identified to prevent inadvertent use.

iii. Distribution

Proposed § 820.124 is a combination of existing §§ 820.150 and 820.151. The present regulation requires only critical device manufacturers to maintain distribution records. Proposed § 820.124 requires all manufacturers to maintain distribution records. This section incorporates ISO 9001 4.15.5 "Delivery." Proposed § 820.124 is a revision of the suggested language in the November 1990 information document and, therefore, some of the comments no longer apply.

37. Most comments on the November 1990 information document that are pertinent to the revised language in proposed § 820.124 were concerned with the imposition of the critical device requirement to maintain distribution records upon all medical devices. One comment suggested clarifying that control numbers are required for critical devices only.

FDA believes it is crucial for the agency to have access to distribution records in order to ensure that manufacturers are properly complying with recall and complaint investigation requirements, and to ensure that all defective devices are withdrawn from points of use.

iv. Installation

Proposed § 820.126 is identical to § 820.152, except that a requirement is added for a record to be maintained of the installation check. Instructions and procedures for installation must include criteria for determining if the installed device(s) is operating properly. A record of the installation check is necessary to provide evidence that the check was made. This proposed revision of § 820.152 was not included in the November 1990 information document and is a supplement to ISO 9001.

L. Packaging and Labeling Control (Subpart L)

Proposed subpart L consists of a revision of existing §§ 820.120 and 820.121 and a duplication of existing § 820.130.

i. Device packaging

Proposed § 820.160 is identical to existing § 820.130. Thus, this section was not included in the November 1990 information document. This section incorporates ISO 9001 4.15.4 "Packaging."

ii. Device labeling

Proposed § 820.162 is a revision of existing § 820.120 and includes the proofreading requirements of existing § 820.121(b). The revision states that, when labels and other labeling are proofread, a record must be made of the activity. A record is necessary to provide evidence that the labeling was proofread. The modification of existing § 820.120 was included in the November 1990 information document and is a supplement to ISO 9001.

38. One comment said that the requirement to allow proofreading should be expanded to allow proofreading of the labeling artwork or specifications, instead of samples. FDA believes it is crucial that the actual labeling is reviewed prior to use to ensure that it is accurate. A significant number of recalls occur each year due to inaccurate labeling (Ref. 4).

iii. Critical devices, labeling

Proposed § 820.165 is identical to existing § 820.121(a). The remaining labeling requirements for critical devices in existing § 820.121(b) and (c) are covered by other proposed sections. As mentioned previously, existing § 820.121(b) is being included in proposed § 820.162. Existing § 820.121(c) is covered by the general requirement of proposed § 820.120 that requires labeling to be stored to prevent "damage, deterioration, or other adverse effects" such as mixups. Proposed § 820.165 was not included in the November 1990 information document and is a supplement to ISO 9001.

39. Several comments said that it should be clarified that traceability or control numbers are required for critical devices only. In response to these comments, a separate section is provided for critical device requirements.

M. Records (Subpart M)

The proposed requirements under subpart M consist of revisions of the existing subpart J of the CGMP regulation.

i. General requirements

A requirement for legibility, traceability, and storage of records, which is not presently contained in existing § 820.180, is added to proposed § 820.180. All records maintained to meet the requirements of the CGMP regulation must be legible and clearly identified as to the entity to which they refer and must be stored in a manner to prevent deterioration, damage, or loss. When required under the regulation, the records maintained must include pertinent subcontractor quality records. Backups are required when records are stored on a computer. The remainder of the requirements in this section are requirements of existing § 820.180. No changes for this section were suggested in the November 1990 information document. This section incorporates the applicable requirements of ISO 9001 4.16 "Quality records." The confidentiality and record retention period requirements remain the same as in the existing CGMP regulation.

ii. Device master record

Proposed § 820.181 is revised to reflect new documentation requirements and use of the term "Quality system." Proposed § 820.181 is a supplement to ISO 9001. Any changes made to the device master record (DMR) must now be controlled as required by proposed § 820.40. Documentation of software design specifications and software source code is added in proposed § 820.181(a). In proposed § 820.181(c), "quality system procedures" replaces the former "quality assurance procedures" and "verification checks and verification apparatus used" replaces the former quality assurance terminology. Validation protocols and validation results must also be included in the DMR as set forth in revised § 820.181(c).

Documentation of installation, maintenance and servicing procedures in the DMR is required under proposed § 820.181(e).

Existing § 820.182 is being removed. These requirements are now being covered by proposed §§ 820.50 and 820.184. The deletion of existing § 820.182 was suggested in the November 1990 information document. No comments were received.

iii. Device history record

The existing requirements of § 820.184 are being revised to include a requirement that the actual labeling used must be included or its location referenced in the device history record.

Suggested language for the revised device history record requirements was included in the November 1990 information document. The language in proposed § 820.184 is a revision of the suggested language in the information document.

40. Comments in response to the November 1990 information document said that the requirement for specific labeling is not necessary if the manufacturer complies with the device master record requirements. FDA disagrees. Many recalls have occurred each year due to incorrect labeling (Ref. 4). Including the specific labeling in the device history record and requiring review of the record will help to ensure that proper labeling is used. The requirements of proposed § 820.184 are a supplement to ISO 9001, although records applicable to the device history record are required throughout ISO 9001.

iv. Complaint files

Proposed § 820.198 sets out the requirements for complaint files. Written procedures must be provided that describe the complaint handling process, that specify the activities to be conducted, and that address all required functions, including: Responsibilities, recordkeeping, complaint investigation, and the identification of events which must be reported under the MDR regulations at part 803. Proposed § 820.198 also clarifies that the requirements of § 820.198 apply not only to the device, but also to the packaging and labeling of a device. In addition to the current CGMP requirement to investigate complaints, proposed § 820.198(b) clarifies that complaint investigations must include a determination of whether there was an actual device failure, a determination of whether the device was involved in an injury or death, and a determination of the relationship of the device to the incident. These proposed clarifications were included in the November 1990 information document. Proposed § 820.198 is a supplement to ISO 9001.

Any complaint that is also reportable under part 803 must meet all the requirements of § 803.26. Firms that receive complaints or reports from user facilities, distributors, or other sources, that do not contain all the data or information required under part 803 or proposed § 820.198 must contact the reporter and either obtain the missing data or document why the missing information cannot be obtained. Followup should include:

(1) Collection, analysis, and testing of defective devices or samples, whenever possible.

(2) Failure analysis or other evaluation necessary to determine assignable cause.

(3) Review of the product's complaint history for the same or similar problems, including any recent changes in design, instructions, or production techniques.

(4) Formulation of approaches to correct any problems found.

Proposed § 820.198 also clarifies that complaints subject to the provisions of the section may be from any source. While copies of complaints may be contained in other files, such as litigation files, to facilitate processing, the original information regarding the complaint must be maintained in the complaint file specified in proposed § 820.198.

The language in proposed § 820.198 also clarifies that the record of investigation must contain the results of the investigation, including the corrective action taken, and must document the reason for a lack of a reply to the complainant. This information is necessary in order to show that a proper investigation was conducted. In addition to the name of the complainant, the complainant's address and phone number must be included in the record of investigation. This information is necessary to facilitate followup of complaints.

When the complaint involves a manufacturing site, a copy of the complaint and the record of the investigation must be transmitted to the manufacturing site. This is necessary to ensure that the actual manufacturer has all of the information relating to the complaint.

41. Several comments in response to the November 1990 information document said that it is not always possible to determine if there was a device failure. If, after adequate investigation, it is not possible to determine if a complaint involved a device failure, FDA believes that the actions taken by the firm and the results should be recorded in the record of investigation.

42. Several comments said that, as worded, the language that requires the corrective action to be recorded implies that every complaint will result in corrective action.

FDA does not believe the language in proposed § 820.198 makes this implication. Each manufacturer should develop a record for recording complaint investigations that includes provisions for recording corrective actions. When no corrective action is taken, the reason must be recorded. Those events that do not require corrective action may be identified in the written complaint processing procedures.

43. Several comments addressed trend analysis. One comment said that trend analysis was good business sense. One comment said that trend analysis should be added to the audit requirements; another said that trend analysis may not always be appropriate and that concern should be oriented toward significant problems, not just recurring problems of no practical significance.

FDA agrees that trend analysis makes good business sense, but has deleted reference to it in proposed § 820.198. However, proposed § 820.100 does require manufacturers to conduct trend analysis of complaints and other sources of quality data to detect systematic quality problems. FDA notes that trend analysis is the accepted method for detecting systemic problems, while the purpose of the quality audit is to periodically evaluate the applicability and effectiveness of the quality system. The evaluation of trend analysis procedures may be part of the overall audit evaluation. Trend analysis of quality data must be a routine function

of the quality system and is subject to FDA review.

44. With respect to maintaining copies of complaints at the manufacturing site, when the formally designated unit for processing complaints is located at a site separate from the actual manufacturing establishment several comments said that only those records of reviews, findings, and corrective actions that result in modifications to manufacturing operations should be maintained at the manufacturing site.

In response to these comments, FDA is revising the language relating to this proposed requirement to state that copies of complaints should be transmitted to and maintained at the manufacturing site when the complaint involves the manufacturing site.

N. Servicing and Returned Devices (Subpart N)

Proposed § 820.200 will require manufacturers who service devices or who authorize agents to service devices to maintain service records and written procedures for implementing the service activity. Service record data must be reviewed for systemic problems, and systemic problems acted upon when detected.

The quality system established by manufacturers who service devices for users must extend to the servicing operation. Information contained in service records is an important source of device experience information that may be used to detect systematic quality problems. Thus, an important part of the program must be the maintenance of servicing records, the periodic review and evaluation of these records, and the feedback of device problems into the quality data analysis program required under proposed § 820.100. Requirements of the quality system which are applicable to servicing include training, quality audit, component and documentation controls, inspection and testing, nonconforming component and device controls, measuring and test equipment controls, purchasing, and records. Controls must be in place that will ensure that serviced devices meet specifications and must include written procedures for managing the servicing activity.

Suggested language for servicing requirements was included in the November 1990 information document. That language was revised to arrive at the language being proposed for § 820.200. This section incorporates ISO 9001 4.19 "Servicing."

45. Several comments to the November 1990 information document wanted to know if the servicing requirements applied to service and repair at a customer's place of business.

FDA considers the proposed servicing requirements to apply to any servicing conducted or controlled by a finished device manufacturer.

46. Several comments said the language that was suggested to revise the CGMP regulation was too detailed and recommended that the ISO 9001 language be used in lieu of the suggested language. FDA agrees with these comments. The language in proposed § 820.200 is revised to eliminate much of the detailed language contained in the November 1990 information document.

As now written, the requirements in proposed § 820.200 specify that each manufacturer must conduct an analysis of service reports to detect systematic quality problems. When a systemic problem is detected, or a problem is detected that involves a death, serious injury, safety hazard, or recurring failure, that problem should be treated as a complaint and processed according to the requirements in proposed § 820.198. When such problems are identified, a determination must be made as to whether the event is reportable under part 803. Therefore, instructions for reporting under the MDR regulation must be provided in the procedures established to manage the servicing activities.

O. Statistical Techniques (Subpart O)

Proposed § 820.250 incorporates ISO 9001 4.20 "Statistical Techniques" and states that, when appropriate, statistical techniques must be applied to ensure the acceptability of process capability and device characteristics. The use of statistical methods can be beneficial in most aspects of data collection, analysis, and application. They may be used in determining process control, forecasting, verification and measurement, or assessment of quality.

When manufacturers develop sampling plans, the plans must be proven to be statistically sound for their intended use. In addition, sampling plans must be periodically reviewed for adequacy, especially when the plans fail to detect nonconformance. Sampling based upon a statistical rationale is now required by §§ 820.81 and 820.160.

The requirements of proposed § 820.250 were not included in their present form in the November 1990 information document. However, reference to the requisite statistical basis for sampling plans was made in that document with respect to the acceptance of components.

V. Statutory Authority and Enforcement

FDA's statutory authority to issue CGMP regulations is derived from sections 501, 502, 515, 518, 519, 520, 701, 704, and 801 of the act (21 U.S.C. 351, 352, 360e, 360h, 360i, 360j, 371, 374, and 381).

Section 701(a) of the act authorizes FDA to promulgate substantive, binding regulations for the efficient enforcement of the act. *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609 (1973); see also *Weinberger* v. *Bentex Pharmaceuticals, Inc.*, 412 U.S. 645, 653 (1973); *National Assn. of Pharmaceutical Manufacturers* v. *FDA*, 637 F.2d 877 (2d Cir. 1981); *National Confectioners Assn.* v. *Califano*, 569 F.2d 690 (D.C. Cir. 1978); *National Nutritional Foods Assn.* v. *Weinberger*, 512 F.2d 688 (2d Cir.), cert. denied, 423 U.S. 827 (1975). Section 520(f)(1)(A) of the act, as amended by section 18(d) of the SMDA, specifically authorizes the agency to promulgate regulations that prescribe, and require conformance to, CGMP for the manufacture, preproduction design validation, packing, storage, and installation of device. Section 519(a) of the act (21 U.S.C. 360i(a)) also authorizes the agency to issue regulations requiring the manufacturers of devices to maintain and provide records to ensure that devices are not adulterated, misbranded, unsafe, or ineffective. FDA's CGMP regulations for medical devices are substantive regulations with the force and effect of law. *United States* v. *Undetermined Quantities of Various Articles of Device * * * Proplast II*, 800 F. Supp. 499, 502 (S.D. Tex. 1992); *United States* v. *789 Cases * * * Latex Surgeons' Gloves*, 799 F. Supp. 1275, 1287 (D.P.R. 1992).

CGMP regulations for medical devices are enforced through sections 301, 302, 303, 304, 501, 502, and 801 of the act (21 U.S.C. 331, 332, 333, 334, 351, 352, 381). Section 501(h) of the act deems a device to be adulterated if the methods, facilities, or controls for the manufacture, packing, storage, or installation of the device do not conform with good manufacturing practice requirements under section 520(f)(1) of the act (*Proplast II*, 800 F. Supp. at 503; *789 Cases*, 799 F. Supp. at 1285). Under section 502(t)(2) of the act, a device is deemed misbranded if there is a failure or refusal to furnish any material or information required by section 519 of the act respecting a device.

Section 301 of the act (21 U.S.C. 331) sets forth prohibited acts. Under section 301(a) of the act, the introduction of an adulterated or misbranded device into

interstate commerce is prohibited. Under section 301(b) of the act, the adulteration or misbranding of a device in interstate commerce is prohibited. Under section 301(k) of the act, any act which results in a device being adulterated or misbranded after its shipment in interstate commerce is prohibited. Section 301(q)(1)(B) of the act prohibits the failure or refusal to furnish any information required by section 519 of the act.

Persons who commit prohibited acts in violation of section 301 of the act may be enjoined under section 302(a) of the act and may be subject to criminal prosecution under section 303 of the act. Devices that are adulterated within the meaning of section 501(h) of the act, or misbranded within the meaning of section 502(t)(2) of the act, are subject to civil sanctions of seizure and condemnation under section 304(a)(2) of the act.

In addition to the criminal and civil enforcement actions mentioned above, section 17 of the SMDA added section 303(f) to the act. Section 303(f) of the act provides that manufacturers, importers, and distributors may be subject to civil penalties for those violations of sections 519(a) or 520(f) of the act that constitute a significant or knowing departure from these requirements or a risk to the public health. Civil penalties may not exceed $15,000 for a single violation, and may not exceed $1,000,000 for all such violations adjudicated in a single proceeding.

VI. Environmental Impact

The agency has determined under 21 CFR 25.24 (a)(8) and (e)(2) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VII. Economic Impact

A. Summary

FDA has examined the costs and benefits of the proposed rule to revise the CGMP regulations covering medical devices (21 CFR part 820) in accordance with Executive Order 12866 and the Regulatory Flexibility Act (Pub. L. 96–354). The detailed data for this analysis were developed by ERG, under contract to FDA, and the full report, "Economic Analysis of Proposed Revisions to the Good Manufacturing Practices Regulation for Medical Devices," is on file at the Dockets Management Branch (address above).

The objective of the proposed rule is to reduce the number of fatalities and injuries attributable to defective medical devices. The U.S. Office of Management and Budget asks that Federal agencies justify new regulations by demonstrating that the problem that the regulation is designed to correct cannot be adequately addressed by other measures. For example, in some circumstances, private markets or industry guidelines can be relied on to abolish unwarranted risks. In this instance, FDA finds that private market incentives do not adequately reduce the risk of design-related device failures, because neither physicians nor consumers have all of the information needed to make adequate judgments of product quality and legal tort remedies, are slow, inefficient, and extremely costly.

The proposed CGMP regulations will extend the manufacturer's quality system in several areas, including design, purchasing, and servicing; and clarify or expand selected existing requirements. It will affect all medical device establishments engaged in the design, manufacture, contract sterilization, and packaging of medical devices. FDA considered two alternative levels of coverage for the preproduction design requirements of the proposal. The first alternative was to require compliance for all medical devices regardless of the potential public health risk. The second alternative was to exempt about 95 percent of the manufacturers of the lower risk, class I, devices from the preproduction design requirements. FDA found that the benefits from subjecting all device establishments, regardless of the class of device manufactured, to the preproduction design elements were not great enough to justify the cost. A summary of the detailed economic analysis of the proposed CGMP regulations is presented below.

Based on the ERG study, the total annual incremental costs to the U.S. industry of the proposed regulation are estimated to be about $84.5 million. These costs would be more than offset, however, by benefits to public health and by economic benefits to the medical device industry. FDA estimates that the benefits to public health would include over 50 fewer deaths and about 1,150 fewer serious injuries per year, which are now attributed to design-related device failures. Studies on the value of a statistical life have reported estimates ranging from $1.6 million to $8.5 million.[1] Assuming an economic value of $5 million per fatality avoided, the monetary value of saving 50 lives each year would be $250 million. Therefore, the value of the public health benefits of preventing deaths alone easily exceeds the cost of compliance. Moreover, additional economic benefits to medical device establishments would result from cost savings due to fewer design-related product recalls, better product quality, and greater productivity. In addition, medical device establishments exporting to the EC would benefit from the harmonization of the CGMP regulation with the ISO 9001 quality standard. Because the EC is adopting ISO 9001 as a basis for its medical device manufacturing quality system, the harmonization of the two quality requirements will eliminate the need for device manufacturers to maintain different quality systems for each market.

FDA supports the ultimate goal of international harmonization of standards and regulations governing medical devices and the eventual mutual recognition of CGMP inspections between major device markets. While achievement of this goal is still in the future, the harmonization of quality standards is an important first step. The Health Industry Manufacturers Association has stated that reciprocity for quality assurance inspections could save the medical device industry millions of dollars as well as provide significant savings to governments.[2]

For individual establishments, the economic impact of the regulation will depend on a number of factors, such as the level of current compliance, the type of activities performed at the establishment, and the nature of the product. On average, the smaller establishments will bear a relatively greater economic burden.

B. Industry Profile

The U.S. medical device industry is among the most competitive sectors in the United States. It is characterized by a large number of innovative firms, many small, that produce an extremely diversified range of products. In 1991, the industry's domestic production was approximately $33.7 billion and accounted for 47.5 percent of total world medical device output.[3] From

[1] Fisher, A., L. Chestnut, and D. Violette, "The Value of Reducing Risks of Death: A Note on New Evidence," *Journal of Policy Analysis and Management*, 8:88–100, 1989.

[2] Gilmartin, R. V., "The Benefits of Cooperation for Industry and Regulators Alike: A Global Perspective," presented at the Third Annual Global Medical Device Conference, October 2, 1992.

[3] Health Industry Manufacturers Association, "The Global Medical Device Report: Markets for Health Care Technology Products," vol. II, Washington, DC, 1992.

1989 to 1992 the average annual growth in medical device shipments was 9.7 percent compared to an average of less than 1 percent for all U.S. manufacturing. The U.S. Department of Commerce projects continued growth in medical device shipments of 3 to 7 percent through 1997.[4]

Exports are an important factor in the competitiveness of the domestic industry. In 1991, exports were $7.9 billion and accounted for about 23 percent of medical device value of shipments, whereas imports were only $4.1 billion or about 12 percent of domestic consumption.[5] With growth in the domestic market for medical devices projected to slow with the advancement of cost containment measures, the export market would take on even greater importance.

Firms in the medical device industry are heterogeneous. They vary in size, product type, product and process technology, and rate of new product introductions. There are over 7,000 medical device establishments involved in the production of approximately 4,000 different types of devices. Sixty-two percent of these establishments are very small (fewer than 20 employees), while 27 percent are of medium-size (20 to 99 employees), 7 percent are large (100 to 249 employees), and 4 percent are very large (250 or more employees). (See Table 1). These size categories were developed to reflect relative size categories within the medical device industry and differ from the Small Business Administration definition of size. Under the Small Business Administration definition, almost all establishments would be small. FDA categorizes devices by class and criticality. Critical devices are defined as any device intended for surgical implant, to sustain life, or whose failure under normal conditions could result in serious injury or death. The distribution of affected establishments that manufacture or develop devices is presented by class and criticality in Table 2. Most of the establishments that manufacture, contract manufacture, or develop specifications produce class II devices (71 percent), while 8 percent produce class III and 21 percent produce class I devices. Only 10 percent of the establishments produce critical devices (a critical device can be class II or class III).

The class of devices manufactured, the extent of an establishment's current compliance with the proposed changes, the rate of new product introductions, and the size of the establishment are factors that affect the cost of compliance for individual establishments. In general, establishments producing class III and critical devices are subject to more stringent and costly premarket review and CGMP requirements but are also more likely to be in greater compliance with the proposed changes to the CGMP regulation. Also, larger establishments tend to have more formal procedures and more layers of management than smaller ones, increasing the cost and complexity of writing and implementing new procedures. However, because of their more formal structure, larger firms have already implemented many of the proposed changes to the CGMP regulations.

The rate of new product introductions has a major effect on the incremental costs of the proposed CGMP regulation. Based on a limited sample of 510(k) and PMA applications, ERG estimated that the average affected medical device establishment submits 1.1 new product applications per year (Table 3). The submittal rate by size of establishment varied from 0.6 applications per year from small and medium-sized establishments to 6.9 applications per year from very large establishments. Because a substantial number of establishments are small, they remain an important source of new product introductions.

The great diversity of this industry makes it extremely difficult to characterize. Medical devices are classified under one of six Standard Industrial Classification (SIC) codes—Surgical and Medical Instruments (3841); Surgical Appliances and Supplies (3842); Dental Equipment and Supplies (3843); X-ray Apparatus and Tubes (3844); Electromedical Equipment (3845); and Ophthalmic Goods (3851). However, many medical devices are produced by establishments whose primary classification is for another SIC, such as in vitro diagnostics (SIC 2835). An earlier FDA study[6] found primary classifications in over 150 different SIC codes for a significant number of manufacturing establishments registered with the agency.

C. Industry Costs

ERG estimated the total annual incremental cost of the proposed changes to the CGMP regulation at $84.5 million. This includes $6.3 million in one-time costs that were annualized over 5 years at a 10 percent discount rate. Table 4 lists the most costly of the new requirements.

Costs were based on the incremental tasks each manufacturer must perform to achieve compliance. To develop these estimates, ERG assembled a team of economists, industrial engineers, and other industry consultants, who addressed each compliance activity in turn, first assessing the state of current practice and next the level and cost of the needed additional tasks. These estimates take into account the added labor and capital resources that would be needed to move from existing compliance levels to new, more stringent levels required under the proposal. For the most part, ERG determined that most very large and large establishments are already in compliance with many of the new requirements and thus would not experience large increases in costs.

The great majority of the costs for all size establishments will be to establish preproduction design controls for new products. Therefore, the more innovative establishments will experience greater compliance costs than the less innovative establishments. The estimated annual preproduction design control costs total $62.1 million, which represents 74 percent of the total annual incremental cost of compliance. The most costly task within the preproduction design category is design verification ($49.2 million), which includes verifying design output. Other costly tasks are design review ($6.4 million), which encompasses conducting and documenting design review meetings; design changes ($4.0 million), which includes drawing, documenting, and maintaining design change procedures; and design and development planning ($2.5 million), which includes drafting and maintaining standardized plans for device design and development. The requirement for extending the quality system audit to new areas of production such as design and servicing ($5.2 million) and establishing greater purchasing controls ($7.9 million) are also relatively high cost items.

The projected average cost per establishment (Table 5) varies substantially across establishment size categories and by product type, design complexity, and innovation rate. For most sectors of the medical device industry (excluding dental and ophthalmics) the average annual incremental cost per establishment is estimated to be: $19,300 for small, $15,800 for medium, $27,800 for large,

[4] U.S. Department of Commerce, "U.S. Industrial Outlook," Washington, DC, 1993.

[5] Health Industry Manufacturers Association, "The Global Medical Device Report: Markets for Health Care Technology Products," vol. I, Washington, DC, 1992.

[6] Food and Drug Administration, "Baseline Data on Medical Device Industries in the Census of Manufacturers," (OPE Study 53), 1980.

and $11,600 for very large establishments. The dental and ophthalmic industries have a lower rate of new product development than other device industries and, therefore, a lower average cost of compliance ($8,800 per establishment versus $18,700).

Because average current compliance rates vary directly with establishment size and the majority of establishments are small, the largest share of the costs are incurred by small establishments, $50.2 million (59 percent), while the smallest share is incurred by very large establishments, $3.1 million (3.7 percent) (Table 6).

D. Benefits From Proposed Changes to the CGMP

The proposed changes to the CGMP regulation will provide public health benefits to medical device users and economic benefits to the medical device industry. Based on its review of medical device recalls over the past 4 years, FDA has estimated that 30 percent of all medical device product recalls are due to inadequate preproduction design controls. It is extremely difficult to judge how many of these recalls could have been avoided, ERG judged that a majority would have been prevented if manufacturers had fully implemented the proposed CGMP design controls.

1. Public Health Benefits

FDA requires manufacturers to submit an MDR when their device is associated with a patient or user death, serious injury, serious illness, or device malfunction. ERG used the MDR database to estimate the public health benefits of the proposed changes to the CGMP regulation. There were over 47,000 MDR's submitted to FDA in 1991. FDA reviews each report for cause and assigns it a code. An MDR is considered closed when the review is completed. At the time of this report, 22,674 of the 1991 MDR's were closed. Of these closed cases, FDA determined that 19 percent of the fatalities and 23 percent of the serious injuries were device-related. The bulk of the remaining incidents were due to user problems, but also include procedural problems and cases where cause could not be clearly established.

To estimate the total number of deaths and serious injuries for 1991 by cause, the MDR's that were still open were distributed across cause codes based on the 1988 through 1991 averages. To estimate the number of deaths and serious injuries due to design-related causes, ERG assumed that the percent of the device-related MDR's that were design-related MDR's was the same as that for recalls (30 percent). Because MDR's are substantially underreported[3], ERG made an upward adjustment in the number of MDR's of 20 percent for fatalities and 40 percent for serious injuries. Based on these assumptions, medical devices contributed to an estimated 72 fatalities and 1,576 serious injuries in 1991 due to design-related problems in class II and class III devices (Table 7).

To develop an approximate idea of the preventability of these incidents, ERG convened a panel of industrial engineers and regulatory specialists with extensive experience in the design of medical devices. Each panel member evaluated a random sample of 100 design-related recalls. ERG found that the expected value of their judgments implied that proper design controls would have prevented about 73 percent of these recalls. Based on this preventability ratio, ERG calculated that the proposal would prevent about 53 deaths and 1,150 serious injuries per year.

To verify the reasonableness of these estimates, FDA examined an alternative method of estimating the number of fatalities caused by design-related device failures. For this calculation, 3 years of design-related recalls were assumed to be linked to MDR fatalities that occurred for these devices 1 year before or 3 months after the date of the recall. This approach, which provides a lower-bound estimate, because not all relevant fatalities and subsequent MDR's would occur during this limited time period, found that about 60 deaths per year were due to design-related device failures. If 73 percent of such incidents could be avoided through compliance with the proposed CGMP regulation, 44 deaths per year would be prevented.

These estimates of the public health benefits from fewer design-related deaths and serious injuries represent FDA's best projections, given the limitations and uncertainties of the data and assumptions. It should be noted that the failure of just one widely used device can cause an exceptionally large number of deaths and injuries. For example over 500 fractures of the Bjork-Shiley convexo-concave heart valve, with over 300 deaths, have been reported since 1980. Worldwide, there are over 56,000 surviving recipients of this device and fractures still occur at a rate of 30 to 40 per year.

Moreover, the above numbers do not capture the quality of life losses to patients who experience less severe injuries than those reported in MDR's, who experience anxiety as a result of diagnosis or treatment with an unreliable medical device, or who experience inconvenience and additional medical costs because of device failure.

Medical device malfunctions are substantially more numerous than deaths or injuries from device failures and also represent a cost to society. Malfunctions represent a loss of product and an inconvenience to users and/or patients. Additionally, medical device malfunctions burden medical personnel with additional tasks, such as repeating treatments, replacing devices, returning and seeking reimbursement for failed devices, and providing reports on the circumstances of medical device failures. No attempt was made to quantify these additional costs.

2. Industry Benefits

The medical device industry would gain substantial economic benefits from the proposed changes to the CGMP regulations in three ways: cost savings from fewer recalls, productivity gains from improved designs, and efficiency gains for export-oriented manufacturers, who would now need to comply with only one set of quality standards.

An average of 359 medical device recall events per year were reported to FDA over the period 1988 to 1991. As stated above, FDA estimates that design-related deficiencies contributed to 30 percent of those recall events annually. Applying the 73 percent recall preventability factor, ERG projects that there would be 67 fewer recalls of class II and class III devices each year under the proposed CGMP regulation (Table 8). Although substantial medical device recall cost data were not available, ERG estimated that if the cost and distribution of medical device recalls were similar to those reported in previous drug and device recall studies, the industry would avoid roughly $45 million worth of recall expenses per year by adopting the new CGMP regulation.

ERG also found that the design control requirements in the proposed CGMP regulation would require manufacturers to integrate their design and production operations and that most industry experts believe that this change would lead to better quality products, more efficient engineering, lower manufacturing costs, and reduced product development time. These savings, however, could not be quantified.

Still another benefit of the revised regulation relates to the harmonization

[3] General Accounting Office, "Medical Devices: Early Warning is Hampered by Severe Underreporting," GAO/PMED-87-1, Washington, DC, 1986.

of the proposed CGMP rule with the ISO 9001 international standard. This change would especially benefit export-oriented establishments, because they would need to meet only one set of quality standards. The EC in particular is important because it is second only to the United States in market size and purchases $3.4 billion (43 percent) of U.S. medical device exports.[8] ERG could not derive quantitative measures of this benefit, however, due to the lack of data regarding implementation of the standard in the EC.

E. Costs and Benefits if all Device Classes Were Subject to Preproduction Design Requirements

If all device classes were subject to the proposed design control requirements the total annualized compliance cost would increase from $84.5 million to $91.3 million (Table 9), solely due to a $6.8 million increase in annualized compliance costs for class I devices. In contrast, ERG estimates that subjecting class I devices to the design control requirements would have no expected impact on the number of fatalities avoided. There would, however, be 108 fewer design-related serious injuries (Table 10) and 11 fewer design-related recalls (Table 11).

F. Economic and Small Business Impact

The ability of medical device establishments to pass on the added cost of the proposed changes will determine their economic impact on the industry. Under the current medical care system, the demand for medical devices tends to be price inelastic because they are often prescribed by physicians and frequently paid for by third parties. Thus, small price increases have not typically prompted significant declines in industry sales. Nonetheless, competitive pressures would rise under new health care cost-containment measures. Therefore, to examine the potential effect of the costs of compliance on the industry's competitive structure, ERG calculated the maximum impact on industry average prices and profits, using extreme scenarios.

Based on the assumption that all costs of compliance are passed through to the end user, with no loss in sales and no offset for avoided recalls or other industry productivity gains, ERG found that the average increase in the price of medical devices would be less than 0.2 percent. Estimated price increases ranged from 0.06 percent for X-ray Apparatus and Tubes (SIC 3844) and Electromedical Equipment (SIC 3845) to 0.24 percent for Dental Equipment and Supplies (SIC 3843) (Table 12). (The maximum price increase was calculated using aggregate compliance costs as a percentage of the value of shipments.) The price increases calculated by size of establishment suggest that small establishments will be under greater pressure to increase prices. The cost of compliance represented an average of 1.8 percent of the value of shipments for small establishments and only 0.01 percent for very large establishments.

To estimate the potential impact of compliance costs on medical device industry profits, ERG calculated after-tax compliance costs as a percentage of after-tax income for each medical device SIC (Table 12). Again, no adjustments were made for avoided recalls or expected productivity gains. If manufacturers have no ability to increase prices to offset the increase in compliance costs, this estimate represents an upper bound of the potential effect on entity income. Under these circumstances, the medical device sectors would incur reductions in net income ranging from about 1 percent (SIC 3844 and 3845, X-ray Apparatus and Tubes and Electromedical Equipment) to about 3 percent (SIC 3843 and 3851, Dental Equipment and Ophthalmic Goods). ERG concluded that such impacts may affect some establishments' decisions to develop new products where expected profits are marginal or highly uncertain, but judged that the level of incremental costs imposed by this regulation would not substantially lower the innovation rate of products with significant medical benefits.

In accordance with the Regulatory Flexibility Act, FDA has considered the effect of this action on small businesses and has determined that there will be a significant impact on a substantial number of small businesses. The increase in costs is greatest for small establishments due to the large number of small establishments in the industry (62 percent are small) and the lower rate of current compliance by small establishments. The actual added cost per establishment will vary by the establishment's current level of compliance, complexity of product design, product type, and rate of product innovation. Small establishments producing differentiated products or marketing to niche markets may not be at a disadvantage because of their ability to pass on the added cost of compliance. However, small establishments that compete with larger establishments based on price alone would suffer a drop in profits if they currently operate at a lower level of compliance than their competitors. For small start-up establishments that have not yet developed significant sales volume, regulatory costs would amount to a substantial fraction of company revenues.

FDA, through its Division of Small Manufacturers Assistance has a number of programs designed to assist small businesses. The Division of Small Manufacturers Assistance provides guidance materials, regional seminars and technical assistance that can help small businesses with their compliance activities. In addition, FDA's decision to exempt the majority of class I device manufacturers from preproduction design requirements decreases the cost of compliance by $6.8 million and minimized the potential burden on small establishments that manufacture class I devices. About 60 percent of that $6.8 million would have been borne by small establishments.

In summary, FDA concludes that the $84.5 million annual incremental cost to comply with the proposed changes to the CGMP regulation would be substantially offset by significant savings from avoided recalls and more importantly, the avoidance of deaths and serious injuries due to design-related device failures or malfunctions. FDA's estimate of public health benefits includes the prevention of about 53 deaths and 1,150 serious injuries annually. In addition, establishing preproduction design controls would result in better designed and higher quality devices and fewer device malfunctions or failures would reduce the inconvenience and expense of repetitive treatments or diagnoses. These public health benefits exceed industry's cost of compliance.

[8] Health Industry Manufacturers Association, "The Global Medical Device Report: Markets for Health Care Technology Products," vol. I, Washington, DC, 1992.

TABLE 1.—DISTRIBUTION OF AFFECTED ESTABLISHMENTS BY EMPLOYMENT SIZE

Type of establishment	Total [1]	Employment size [2]			
		Small (1–19)	Medium (20–99)	Large (100–249)	Very large (≥250)
Manufacturer	5,415	3,323	1,414	415	265
Contract manufacturer	419	257	109	32	20
Specification developer	541	352	162	27	0
Repacker/relabeler	828	538	248	41	0
Contract sterilizer	34	22	10	2	0
Total	7,237	4,492	1,943	517	285

[1] Based on data from FDA's Registration and Listing Branch, 1992, adjusted to reflect 13 percent not required to register and 6 percent exempt from CGMP requirements.
[2] ERG, Section 3.

TABLE 2.—DISTRIBUTION OF ESTABLISHMENTS BY HIGHEST CLASS OF MEDICAL DEVICE MANUFACTURED

Type of establishment	Total [1]	Class [2]			Noncritical	Critical
		I	II	III		
Manufacturer	5,415	1,137	3,844	433	4,873	541
Contract manufacturer	419	88	297	33	377	42
Specification developer	541	114	384	43	487	54
Total	6,375	1,339	4,525	510	5,737	637

[1] Includes manufacturing and product development establishments only.
[2] The Evolving Medical Device Industry 1976 through 1984. OPE, FDA (OPE study 74).
Note: Totals may not add due to rounding.

TABLE 3.—Annual Number of 510(K) AND PMA SUBMISSIONS PER ESTABLISHMENT

	Total	Employment size			
		Small (1–19)	Medium (20–99)	Large (100–249)	Very large (≥250)
Average number of product submissions	[1] 6,317	2,264	885	1,342	1,826
Number of affected establishments	[2] 5,956	3,675	1,576	442	265
Average number of 510(k) and PMA submissions per establishment	1.1	0.6	0.6	3.0	6.9

[1] Number includes 50 percent of PMA supplements.
[2] The number of manufacturers and the number of specification developers that would incur design costs associated with new product introduction.
Source: ERG, Section 3.

TABLE 4.—TOTAL COMPLIANCE COSTS BY MOST COSTLY INCREMENTAL TASKS

[$ millions]

Incremental tasks	One-time annualized [1]	Annual		Total annualized
		Labor	Nonlabor	
Preproduction design:				
Design verification	NA	19.7	29.5	49.2
Design review	NA	6.4	NA	6.4
Design changes	0.1	3.9	NA	4.0
Design and development planning	0.9	1.6	NA	2.5
Other:				
Quality audit	0.5	4.7	NA	5.2
Purchasing controls	0.6	4.7	2.6	7.9
Management review	NA	2.2	NA	2.2
Corrective action	0.9	0.3	NA	1.2
All remaining	3.3	2.0	0.5	5.9
Total of proposed regulation	6.3	45.5	32.6	84.5

[1] One-time costs annualized over 5 years at discount rate of 10 percent.
Notes: NA = Not Applicable; Totals may not add due to rounding; Source: ERG, Section 4.

TABLE 5.—TOTAL ANNUALIZED [1] AVERAGE COSTS PER ESTABLISHMENT BY EMPLOYMENT SIZE

Establishment employment size	Medical and surgical instruments, x-ray, and electromedical device industries (SIC 3841, 3842, 3844, and 3845) (dollars)	Dental and ophthalmic industries (SIC 3843 and 3851) (dollars)
Small (1–19)	19,300	7,700
Medium (20–99)	15,800	8,700
Large (100–249)	27,800	16,300
Very large (≥ 250)	11,600	11,600
All establishments	18,700	8,800

[1] One-time costs annualized over 5 years at discount rate of 10 percent.
Source: ERG, Section 6.

TABLE 6.—TOTAL ANNUALIZED COSTS BY SIZE CATEGORY

[$ millions]

Establishment size	One-time annualized [1]	Annual		Total annualized
		Labor	Nonlabor	
Small (1–19)	3.2	26.0	21.0	50.2
Medium (20–99)	2.0	11.3	7.7	21.0
Large (100–249)	0.7	5.8	3.8	10.2
Very large (≥ 250)	0.5	2.5	0.1	3.1
All establishments	6.3	45.6	32.6	84.5

[1] One-time costs annualized over 5 years at discount rate of 10 percent.
Notes: Totals may not add due to rounding; Source: ERG, Section 4.

TABLE 7.—NUMBER OF DESIGN-RELATED REPORTS AND ESTIMATED AVOIDED DEATHS AND SERIOUS INJURIES

	Fatalities			Serious injuries		
	Class II	Class III	Total	Class II	Class III	Total
Number in 1991	551	482	1,033	4,269	12,175	16,444
Device-related	124	76	200	538	3,214	3,752
Design-related [1]	37	23	60	161	964	1,126
Adjusted total number of design-related MDR's [2]	45	27	72	226	1,350	1,576
Number avoided	33	20	53	165	984	1,149

[1] Assumes 30 percent of device-related MDR's are design-related, based on FDA recall data.
[2] Total number of fatalities and injuries increased by 20 and 40 percent, respectively, to adjust for underreporting.
Source: ERG, Section 5.

TABLE 8.—NUMBER OF AVOIDED DESIGN-RELATED RECALL EVENTS BY CLASS OF DEVICE

Device Class	Average number of design-related recall events [1]	Number of avoided design-related recall events [2]
I	16	NA
II	79	58
III	12	9
All devices	107	67

[1] Office of Compliance and Surveillance, CDRH.
[2] ERG estimates based on random sample of recent design-related recalls.

TABLE 9.—TOTAL ANNUALIZED [1] COST BY DEVICE CLASS FOR PROPOSAL AND ALTERNATIVE

[$ millions]

Device class	Proposal		Alternative	
	Annualized costs	Percent of total	Annualized costs	Percent of total
Class I	5.2	6	11.9	13
Class II	71.4	85	71.4	78
Class III	7.9	9	7.9	9

TABLE 9.—TOTAL ANNUALIZED [1] COST BY DEVICE CLASS FOR PROPOSAL AND ALTERNATIVE—Continued

[$ millions]

Device class	Proposal		Alternative	
	Annualized costs	Percent of total	Annualized costs	Percent of total
Total	84.5	100	91.3	100

[1] One-time costs annualized over 5 years at discount rate of 10 percent
Source: ERG, Section 4.

TABLE 10.—NUMBER OF DESIGN-RELATED REPORTS AND ESTIMATED AVOIDED DEATHS AND SERIOUS INJURIES WHEN ALL DEVICES ARE SUBJECT TO DESIGN CONTROLS

	Fatalities				Serious injuries			
	Class I	Class II	Class III	Total	Class I	Class II	Class III	Total
Number in 1991	38	551	482	1,071	1,092	4,269	12,175	17,536
Device-related	1	124	76	201	355	538	3,214	4,107
Design-related [1]	<1	37	23	60	106	161	964	1,232
Adjusted total number of design-related MDR's [2]	<1	45	27	72	148	226	1,350	1,725
Number avoided	<1	33	20	53	108	165	984	1,257

[1] Assumes 30 percent of device-related MDR's are design-related, based on FDA recall data.
[2] Total number of fatalities and injuries increased by 20 and 40 percent, respectively, to adjust for underreporting.

TABLE 11.—NUMBER OF AVOIDED DESIGN-RELATED RECALL EVENTS BY CLASS OF DEVICE WHEN ALL DEVICES ARE SUBJECT TO DESIGN CONTROLS

Device class	Average number of design-related recall events [1]	Number of avoided design-related recall events [2]
I	16	11
II	79	58
III	12	9
All devices	91	78

[1] Office of Compliance and Surveillance, CDRH.
[2] ERG estimates based on random sample of recent design-related recalls.
Source: ERG, Section 5.

TABLE 12.—MAXIMUM POTENTIAL IMPACT ON PRICE OR PROFITS BY INDUSTRY AND EMPLOYMENT SIZE

Industry	Total annualized compliance costs as a percentage of shipments	After-tax compliance costs as a percentage of after-tax income
3841 Surgical and medical instruments	0.15	2.41
3842 Surgical appliances and supplies	0.18	2.29
3843 Dental equipment and supplies	0.24	3.02
3844 X-ray apparatus and tubes	0.06	1.10
3845 Electromedical equipment	0.06	0.88
3851 Ophthalmic goods	0.20	3.00
All	0.15	2.11
Establishment size:		
Small (1–19)	1.78	NA
Medium (20–99)	0.23	NA
Large (100–249)	0.11	NA
Very large (≥250)	0.01	NA
All	0.15	NA

Notes: NA=not available; Source: ERG, Section 5.

VIII. Paperwork Reduction Act of 1980

This proposed rule contains information collections that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1980 (44 U.S.C. chapter 35). The title, description, and respondents of the information collection are shown below with an estimate of the annual recordkeeping burden.

Title: Medical Devices, Current Good Manufacturing Practice Regulations,

Proposed Revisions, Request for Comments.

Description: FDA is proposing to revise the CGMP regulations for medical devices in part 820. Changes proposed include revisions that would: Replace quality assurance program requirements with quality system requirements, including design, procurement and servicing controls; eliminate critical component and critical operation terminology; expand procedures for device failure and complaint investigations; clarify requirements to qualify, verify, and validate processes and changes; and, clarify requirements to evaluate quality data and correct quality problems. Through reorganization and modification of terms, the revised CGMP requirements for medical devices are compatible with specifications for quality systems contained in international quality standards, ISO 9001/EN 29001, "Quality Systems Part 1. Specification for design/development, production, installation and servicing."

Description of Respondents: Businesses or other for-profit and small businesses or organizations.

ESTIMATED ANNUAL BURDEN FOR RECORDKEEPING

Part	Annual no. of recordkeepers	Annual hours per recordkeeper	Total recordkeeping hours
820	7,237	55.880842	404,410

Under OMB information collection No. 0910–0073, an estimated 375,266 burden hours have already been approved for 21 CFR part 820. The information requirements contained in this proposed rule will add 463,128 hours to the burden estimate.

As required by section 3504(h) of the Paperwork Reduction Act, FDA is submitting to OMB a request that it approve these information collection requirements. Organizations and individuals desiring to submit comments for consideration by OMB on these information collection requirements, should direct them to FDA's Dockets Management Branch (address above) and to the Office of Information and Regulatory Affairs, Office of Management and Budget, rm. 3001, New Executive Office Bldg., 725 17th St. NW., Washington, DC 20503, Attn: Desk Officer for FDA.

IX. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. ISO 9001/EN 29001 "Quality Systems Part 1. Specification for Design/Development, Production, Installation, and Servicing," International Organization for Standardization, 1987.

2. "Suggested Changes to the Medical Device Good Manufacturing Practices Regulation Information Document November 1990," FDA, Center for Devices and Radiological Health, Rockville, MD 20857, Docket No. 90N–0172.

3. "Device Recalls: A Study of Quality Problems," FDA, Center for Devices and Radiological Health, Rockville, MD 20857, HHS Publication FDA 90–4235, January 1990.

4. "Preproduction Quality Assurance Planning; Recommendations for Medical Device Manufacturers," FDA, Center for Devices and Radiological Health, Rockville, MD 20857, HHS Publication FDA 90–4236, September 1989.

5. "Software Related Recalls for Fiscal Years FY 83–FY 91," FDA, Center for Devices and Radiological Health, Rockville, MD 20857, May 1992.

6. "FDA Medical Device Regulation From Premarket Review to Recall," Office of Inspector General, Washington, DC, HHS Publication OEI 09–90–00040, February 1991.

7. Letter from American Cyanamid Company to Dockets Management Branch (HFA–305), in response to Docket No. 90N–0172, February 28, 1991.

8. Letter from XRE Corporation to Dockets Management Branch (HFA–305) in response to Docket No. 90N–0172, August 16, 1990.

9. "Guideline on General Principles of Process Validation," FDA, Center for Drugs and Biologics, and Center for Devices and Radiological Health, Rockville, MD 20857, May 1987.

10. EN46001 "Quality Systems—Medical Devices—Particular Requirements for the Application of EN29001."

11. EN46002 "Quality Systems—Medical Devices—Particular Requirements for the Application of EN29002."

12. ISO 8402 "Quality Vocabulary," International Organization for Standardization, 1986.

13. "Management Practices; U.S. Companies Improve Performance Through Quality Efforts," General Accounting Office, Washington, DC 20548, May 1991, GAO/NSLAD–91–190.

14. "Economic Analysis of Proposed Revisions to the Good Manufacturing Practices Regulation for Medical Devices," FDA Contract No. 223–91–8100, Eastern Research Group, Inc., Lexington, MA 02173.

X. Request for Comments

Interested persons may, on or before February 22, 1993, submit to the Dockets Management Branch (address above) written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

FDA is establishing a 120-day comment period, rather than its usual 60 days, in anticipation that the agency will be requested to extend the comment period. The agency will not entertain requests to extend the comment period further.

List of Subjects in 21 CFR Part 820

Medical devices, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 820 be revised to read as follows:

PART 820—GOOD MANUFACTURING PRACTICE FOR MEDICAL DEVICES

Subpart A—General Provisions

Sec.

820.1 Scope.
820.3 Definitions.
820.5 Quality system.

Subpart B—Quality System Requirements

820.20 Management responsibility.
820.22 Quality audit.
820.25 Personnel.

Subpart C—Design Controls

820.30 Design controls.

Subpart D—Document and Record Controls

820.40 Document controls.

Subpart E—Purchasing Controls

820.50 Purchasing controls.

Subpart F—Identification and Traceability

820.60 Identification and traceability.
820.65 Critical devices, traceability.

Subpart G—Production and Process Controls

820.70 Production and process controls.
820.75 Special processes.

Subpart H—Inspection and Testing

820.80 Inspection and testing.
820.84 Inspection, measuring, and test equipment.
820.86 Inspection and test status.

Subpart I—Nonconforming Components and Devices

820.90 Nonconforming components and devices.
820.91 Nonconforming components and devices, critical devices.

Subpart J—Corrective Action

820.100 Corrective action.

Subpart K—Handling, Storage, Distribution, and Installation

820.120 Handling.
820.122 Storage.
820.124 Distribution.
820.126 Installation.

Subpart L—Packaging and Labeling Control

820.160 Device packaging.
820.162 Device labeling.
820.165 Critical devices, labeling.

Subpart M—Records

820.180 General requirements.
820.181 Device master record (DMR).
820.184 Device history record.
820.198 Complaint files.

Subpart N—Servicing

820.200 Servicing.

Subpart O—Statistical Techniques

820.250 Statistical techniques.

Authority: Secs. 501, 502, 510, 513, 514, 515, 518, 519, 520, 522, 701, 704, 801, 803 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351, 352, 360, 360c, 360d, 360e, 360h, 360i, 360j, 360l, 371, 374, 381, 383).

Subpart A—General Provisions

§ 820.1 Scope.

(a) *Applicability.* (1) The regulations set forth in this part describe current good manufacturing practices (CGMP's) for methods used in, and the facilities and controls used for, the design, purchasing, manufacture, packaging, labeling, storage, installation, and servicing of all finished devices intended for human use. The regulations in this part are intended to ensure that finished devices will be safe and effective and otherwise in compliance with the Federal Food, Drug, and Cosmetic Act (the act). This part establishes minimum requirements applicable to manufacturers of finished devices, including additional requirements for critical devices. With respect to class I devices, design controls apply only to those devices listed in § 820.30(a)(2). The regulations in this part do not apply to manufacturers of components or parts of finished devices when such components or parts are not intended specifically for use as part of a medical device, but such manufacturers are encouraged to use appropriate provisions of this regulation as guidelines. Manufacturers of human blood and blood components are not subject to this part, but are subject to part 606 of this chapter.

(2) The provisions of this part shall be applicable to any finished device, as defined in this part, intended for human use, that is manufactured, imported, or offered for import in any State or Territory of the United States.

(b) *Limitations.* The CGMP regulation in this part supplements regulations in other parts of this chapter except where explicitly stated otherwise. In the event it is impossible to comply with all applicable regulations, both in this part and in other parts of this chapter, the regulations specifically applicable to the device in question shall supersede any other regulations.

(c) *Consequences of failure to comply with the regulations.* (1) The failure to comply with any applicable provision in this part in the design, purchasing, manufacture, packaging, labeling, storage, installation, or servicing of a device renders the device adulterated under section 501(h) of the act. Such a device, as well as any person responsible for the failure to comply, is subject to regulatory action under sections 301, 302, 303, 304, and 801 of the act.

(2) If a manufacturer who imports devices into the United States refuses to schedule an FDA inspection of a foreign facility for compliance with this part or refuses to permit FDA to conduct or complete a scheduled inspection at a foreign facility, it shall appear, for purposes of 801(a) of the act, that the methods used in, and the facilities and controls used for, the design, purchasing, manufacture, packaging, labeling, storage, installation, or servicing of any devices produced at such facility that are offered for import into the United States do not conform to the requirements of section 520(f) of the act and this part and that the devices manufactured at that facility are adulterated under section 501(h) of the act. Foreign CGMP inspections will be scheduled in advance by FDA in writing.

(d) *Exemptions or variances.* Any person who wishes to petition for an exemption or variance from any device good manufacturing practice requirement is subject to the requirements of section 520(f)(2) of the act. Petitions for an exemption or variance shall be submitted according to the procedures set forth in § 10.30 of this chapter, the Food and Drug Administration's administrative procedures. Guidance is available from the Center for Devices and Radiological Health, Division of Small Manufacturers Assistance, Regulatory Assistance Branch (HFZ–220), 1901 Chapman Ave., Rockville, MD 20857, telephone 1–800–638–2041. Maryland and foreign residents, 1–301–443–6597, FAX 301–443–8818.

§ 820.3 Definitions.

(a) *Act* means the Federal Food, Drug, and Cosmetic Act, as amended (secs. 201–903, 52 Stat. 1040 et seq., as amended (21 U.S.C. 321–394)). All definitions in section 201 of the act shall apply to these regulations.

(b) *Complaint* means any written, electronic, or oral communication that relates to or concerns the unacceptability of the identity, quality, durability, reliability, safety, effectiveness, or performance of a device.

(c) *Component* means any raw material, substance, piece, part, software, firmware, packaging, labeling, or assembly used during device manufacture which is intended to be included as part of the finished, packaged, and labeled device.

(d) *Control number* means any distinctive combination of letters or numbers, or both, from which the complete history of the purchasing, manufacturing, packaging, labeling, and distribution of a lot or batch of finished devices can be determined.

(e) *Critical device* means a device that is intended to be surgically implanted into the body or to support or sustain life the failure of which to perform when properly used in accordance with instructions for use provided in the labeling can be reasonably expected to result in a serious injury to the user. Examples of critical devices are identified by the Commissioner of Food and Drugs after consultation with the Device Good Manufacturing Practice Advisory Committee authorized under section 520(f) of the act, and an illustrative list of critical devices is available from the Center for Devices and Radiological Health, Food and Drug Administration, at the addresses given in § 820.1(d).

(f) *Design history record* means a compilation of records containing the complete design history of a finished device.

(g) *Design input* means the physical and performance requirements of a device that are used as a basis for device design.

(h) *Design output* means the results of a design effort at each design phase and at the end of the total design effort. The total finished design output consists of the device, its packaging and labeling, and the associated specifications and drawings and the production and quality system specifications and procedures which are included in the device master record (DMR).

(i) *Design review* means a comprehensive, systematic examination of a design to evaluate the adequacy of the device requirements, to evaluate the capability of the design to meet these requirements, and to identify problems with the design and design requirements and to propose solutions to all such problems.

(j) *Device history record* means a compilation of records containing the complete production history of a finished device.

(k) *Device master record (DMR)* means a compilation of records containing a device's complete design, formulation, and specifications, the purchasing and manufacturing procedures and specifications, the quality system requirements and procedures, and the packaging, labeling, servicing, maintenance, and installation procedures of a finished device.

(l) *Establish* means define, document, and implement.

(m) *Executive management* means those senior employees of a manufacturer who have the authority to establish or make changes to the manufacturer's quality policy, quality system requirements, or to a device's design specifications or its production, distribution, servicing, maintenance, or installation procedures.

(n) *Finished device* means any device or accessory to any device that is suitable for use, whether or not it is packaged or labeled for commercial distribution. A finished device includes a device that is intended to be sterile that is not yet sterilized.

(o) *Lot or batch* means a unit of components or finished devices that consists of a single type, model, class, size, composition, and software version that are manufactured under essentially the same conditions and that are intended to have uniform character and quality within specified limits.

(p) *Manufacturer* means any person who designs, manufactures, fabricates, assembles, or processes a finished device, including contract sterilizers, specification developers, repackers, relabelers, and initial distributors of imported devices.

(q) *Manufacturing material* means any material or substance used in, or to facilitate, a manufacturing process that is not intended by the manufacturer to be included in the finished device, including cleaning agents, mold-release agents, lubricating oils, ethylene oxide or other sterilant residues, or other byproducts of the manufacturing process.

(r) *Nonconforming* means the failure of a component, manufacturing material, or finished device to meet its specifications, either before or after distribution of the finished device.

(s) *Production* means all activities subsequent to design transfer and to the point of distribution.

(t) *Quality* means the totality of features and characteristics that bear on the ability of a device to satisfy fitness-for-use, including safety and performance.

(u) *Quality audit* means an established systematic, independent, examination of a manufacturer's entire quality system that is performed at defined intervals and at sufficient frequency to ensure that both quality system activities and the results of such activities comply with specified quality system procedures, that these procedures are implemented effectively, and that these procedures are suitable to achieve quality system objectives. "Quality audit" is different from, and in addition to, the other quality system activities required by or under this part.

(v) *Quality policy* means the overall quality intentions and direction of an organization with respect to quality, as formally expressed by executive management.

(w) *Quality system* means the organizational structure, responsibilities, procedures, specifications, processes, and resources for implementing quality management.

(x) *Record* means any written or automated document, including specifications, procedures, protocols, standards, methods, instructions, plans, files, forms, notes, reviews, analyses, and reports.

(y) *Reprocessing* means all or part of a manufacturing operation which is intended to correct nonconformance in a component or finished device.

(z) *Servicing* means maintenance or repair of a finished device for purposes of returning a device to its specifications.

(aa) *Special process* means any process the results of which cannot be completely verified by subsequent inspection and testing.

(bb) *Specifications* means the documents that prescribe the requirements with which a device, component, production or servicing activity, or quality system must conform.

(cc) *Validation* means, with respect to a device, establishing and documenting evidence that the device is fit for its intended use. With respect to a process, "validation" means establishing and documenting evidence that the process will consistently produce a result or product meeting its predetermined specifications and quality attributes.

(dd) *Verification* means confirming and documenting, with valid, objective evidence, that specified requirements have been met. Verification includes the process of examining the results of an activity to determine conformity with the stated specifications for that activity and ensuring that the device is adequate for its intended use.

§ 820.5 Quality system.

Each manufacturer shall establish and maintain a quality system that ensures that the requirements of this part are met, and that devices produced are safe, effective, and otherwise fit for their intended uses. As part of its quality system activities, each manufacturer shall:

(a) Establish effective quality system instructions and procedures in accordance with the requirements of this part; and

(b) Maintain the established quality system instructions and procedures effectively.

Subpart B—Quality System Requirements

§ 820.20 Management responsibility.

(a) *Quality policy.* Each manufacturer's executive management shall establish its policy and objectives for, and commitment to, quality. Executive management shall maintain the policy at all levels in the organization. Executive management shall ensure that this policy is understood by all employees who may affect or influence the quality of a device.

(b) *Organization.* Each manufacturer shall establish and maintain an adequate organizational structure with sufficient personnel to ensure that devices are produced in accordance with the requirements of this part.

(1) Responsibility and authority. With respect to each section in this part, each manufacturer shall establish the responsibility, authority, and interrelation of all personnel who manage, perform, and verify work

affecting quality, particularly for personnel who need the organizational freedom and authority to:

(i) Initiate or implement action to prevent the occurrence or use of nonconforming components, manufacturing materials, or finished devices;

(ii) Identify or document quality problems with devices, production, or the quality system;

(iii) Initiate, recommend, provide, or implement solutions or corrective actions to quality problems;

(iv) Verify the adequacy or implementation of solutions or corrective actions to quality problems; and

(v) Direct or control further processing, distribution, or installation of nonconforming components, manufacturing materials, or finished devices.

(2) Verification resources and personnel. Each manufacturer shall establish verification functions and shall provide adequate resources and assign adequately trained personnel to perform verification activities.

(3) Management representative. Each manufacturer's executive management shall appoint an individual in executive management, who irrespective of other responsibilities, shall have established authority over and responsibility for:

(i) Ensuring that quality system requirements are established and maintained in accordance with this part; and

(ii) Reporting on the performance of the quality system to executive management for review and to provide information for improvement of the quality system; and the appointment shall be documented.

(c) *Management review.* Each manufacturer's executive management shall review the suitability and effectiveness of the quality system at defined intervals and at sufficient frequency to ensure that the quality system satisfies the requirements of this part and the manufacturer's established quality policy objectives. The management review shall be conducted in accordance with established review procedures, and the results of each quality system review shall be documented.

§ 820.22 Quality audit.

(a) Each manufacturer shall conduct quality audits to verify that the quality system is in compliance with the established quality system requirements. Quality audits shall be conducted in accordance with established audit procedures by appropriately trained individuals who do not have direct responsibilities for the matters being audited. A report of the results of each quality audit shall be made and the audit reports shall be reviewed by management having responsibility for the matters audited. Followup corrective action, including reaudit of deficient matters, shall be taken when necessary and shall be documented in the audit report.

(b) Section 820.180 does not apply to quality audit reports required under this section, except reports written to satisfy § 820.50(a), but does apply to established quality audit procedures. Audit reports written as part of the assessment of suppliers or contractors (§ 820.50(a)) are subject to review and copying by FDA. Upon request of a designated employee of the Food and Drug Administration, an employee in executive management shall certify in writing that the audits of the quality system required under this section have been performed and documented and that any required corrective action has been taken.

§ 820.25 Personnel.

(a) *General.* Each manufacturer shall employ sufficient personnel with the necessary education, background, training, and experience to ensure that all activities required by this part are correctly performed.

(b) *Training.* Each manufacturer shall ensure that all personnel are trained to adequately perform their assigned responsibilities. Training shall be conducted in accordance with established procedures by qualified individuals to ensure that employees have a thorough understanding of their current job functions and with the CGMP requirements applicable to their job functions. As part of their training, all employees shall be made aware of device defects which may occur from the improper performance of their specific jobs. Personnel who perform verification activities shall be made aware of defects and errors that may be encountered as part of their verification functions. Employee training shall be documented.

(c) *Consultants.* (1) Each manufacturer shall ensure that any consultant advising on the methods used in, or facilities or controls used for, the design, purchasing, manufacture, packaging, labeling, storage, installation, or servicing of devices has sufficient qualifications (education, training, and experience) to advise on the subjects about which the consultant will advise.

(2) Each manufacturer shall maintain records pertaining to each consultant. Such records shall include the consultant's name and address, the consultant's qualifications, including a copy of the curriculum vitae and a list of previous jobs, and a specific description of the subjects on which the consultant advised.

Subpart C—Design Controls

§ 820.30 Design controls.

(a) *General.* (1) Each manufacturer of any class III, or class II device, and the class I devices listed in paragraph (a)(2) of this section shall establish and maintain procedures to control and verify the design of the device in order to ensure that specified design requirements are met.

(2) The following class I devices are subject to design controls:

Section	Device
862.2050 through 862.2920.	Instruments, Clinical Laboratory.
868.6810	Catheter, Tracheobronchial Suction.
878.4460	Glove, Surgeon's.
880.4680	Apparatus, Single Patient, Portable Suction.
880.6760	Restraint, Protection.
892.1100	Camera, Scintillation (gamma).
892.1110	Camera, Positron.
892.1130	Counter, Whole Body, Nuclear.
892.1300	Scanner, Rectilinear, Nuclear.
892.1320	Probe, Uptake, Nuclear.
892.1330	Scanner, Rectilinear, Nuclear.
892.1410	Synchronizer, Electrocardiograph, Nuclear.
892.1970	Synchronizer, Radiographic, ECG/Respirator.
892.5650	System, Applicator, Radionuclide, Manual.
892.5740	Source, Radionuclide, Teletherapy.

(b) *Design and development planning.* Each manufacturer shall establish and maintain plans that identify each design and development activity and the persons responsible for each activity. The plans shall describe or reference the description of these design and development activities, including any interaction between or among different organizational and technical groups. The plans shall be updated as design and development evolves.

(c) *Design input.* Each manufacturer shall establish design input requirements relating to a device. The design input requirements shall completely address the intended use of the device, including the needs of the user and patient, and shall be reviewed and approved by a designated qualified individual. The approval of design input requirements, including the date and the person(s) approving the requirements, shall be documented.

(d) *Design verification.* Each manufacturer shall establish and maintain procedures for verification of the device design and assign such functions to competent personnel. Design verification shall be performed in a timely manner and shall confirm that design output meets the design input requirements and that the design is adequate for its intended use. The results of the design verification, including identification of the design verified, verification method(s), the date, and the person(s) performing the verification shall be documented in the design history record. Where applicable, design verification shall include software validation and hazard analysis.

(e) *Design review.* Each manufacturer shall conduct a formal design review of the design output according to established procedures. Each manufacturer shall assign design review responsibility to qualified individuals who do not have direct responsibility for the design development. The assignments shall be documented. The results of a design review shall be documented in the design history record.

(f) *Design output.* Each manufacturer shall define and document design output in terms that allow an adequate evaluation of conformance to design input requirements. Design output shall meet the design input requirements and shall include those design characteristics that are essential for the intended use of the device.

(g) *Design transfer.* Each manufacturer shall establish and maintain procedures to ensure that the design basis for a device and its components are correctly translated into production specifications. The production specifications shall be approved by an individual designated by the manufacturer. The approval, including identification of the design, the date, and the person(s) approving the specifications, shall be documented. Each manufacturer shall select a representative sample of a device from the first three production lots or batches and test such sample under actual or simulated use conditions. Each manufacturer shall conduct such testing according to established procedures and shall maintain records of all results of the testing. Each manufacturer shall also conduct such testing when changes are made in the device or manufacturing process.

(h) *Design release.* Each manufacturer shall ensure that a design is not released for production until the design is approved by individuals designated by the manufacturer. The designated individuals shall review all records required for the design history record to ensure that the design history file is complete and that the final design is consistent with the approved design plan before releasing the design. The release, including the date and signature of the individual(s) approving release, shall be documented.

(i) *Design changes.* Each manufacturer shall establish and maintain procedures for the identification, documentation, validation, review, and approval of design changes.

(j) *Design history record.* Each manufacturer shall establish and maintain a design history record for each device. Each design history record shall contain or reference all records necessary to demonstrate that the design was developed in accordance with the approved design plan and the requirements of this part.

Subpart D—Document and Record Controls

§ 820.40 Document controls.

Each manufacturer shall establish and maintain document control procedures to ensure that all documents that must be established and maintained under this part meet the requirements of this part and are accurate and adequate for their intended use.

(a) *Document approval and issue.* Each manufacturer shall designate individuals to review and approve all documents established under this part for adequacy prior to issuance. The approval, including the date and signature of the individual(s) approving the document, shall be documented.

(b) *Document distribution.* Each manufacturer shall ensure that all documents are current and available at all locations for which they are designed, and that all unneeded or obsolete documents are removed from all points of use in a timely manner.

(c) *Documentation changes.* Changes to specifications, methods, or procedures for components, finished devices, manufacturing materials, production, installation, servicing, or the quality system shall be documented, reviewed, and approved by individuals in the same functions/organizations that performed the original review and approval unless specifically designated otherwise. In addition, any change to a specification, method, or procedure that may affect quality shall be validated as adequate for their intended use before approval and issuance. Validation results shall be recorded. Approved changes shall be communicated to the appropriate personnel in a timely manner. When changes are made to a specification, method, or procedure, each manufacturer shall evaluate the change in accordance with an established procedure to determine if the submission of a premarket notification (510(k)) under § 807.81(a)(3) of this chapter, or the submission of a supplement to a premarket approval application (PMA) under § 814.39(a) of this chapter is required, as applicable. Records of this evaluation and its results shall be maintained.

(d) *Documentation change records.* Each manufacturer shall maintain records of changes to documents. Documentation change records shall include a description of the change, identification of the affected documents, the signature of the approving individuals, the approval date, and the date the change becomes effective. A list, index, or equivalent document control procedure shall be established and maintained to identify the current revision of documents in order to ensure that only current, approved documents are in use.

Subpart E—Purchasing Controls

§ 820.50 Purchasing controls.

Each manufacturer shall establish and maintain procedures to ensure that all components, manufacturing materials, and finished devices that are manufactured, processed, labeled, or packaged by other persons or held by other persons under contract conform to specifications. Each manufacturer shall also ensure that services provided by other persons conform to specifications.

(a) *Assessment of suppliers and contractors.* Each manufacturer shall establish and maintain assessment criteria for suppliers and contractors that specify the requirements, including quality requirements that suppliers and contractors must meet. Each manufacturer shall assess and select potential suppliers and contractors on the basis of their ability to meet requirements, including quality requirements and shall establish and maintain a list of suppliers and contractors that meet the manufacturer's documented assessment criteria. Records of the assessment, and assessment results shall be maintained.

(b) *Purchasing forms.* Each manufacturer shall establish and maintain purchasing forms that clearly describe or reference the specifications, including quality requirements, for the components, manufacturing materials, finished devices, or services ordered or contracted for. Purchasing forms shall include an agreement that the suppliers agree to notify the manufacturer of any changes in the product or service so that manufacturers may determine whether

the change may affect the quality of a finished device. Each manufacturer shall review and approve purchasing documents prior to release. The approval, including the date and signature of the individual(s) approving the form, shall be documented.

Subpart F—Identification and Traceability

§ 820.60 Identification and traceability.

Each manufacturer shall establish and maintain procedures for identifying components, manufacturing materials, and finished devices during all stages of production, distribution, and installation to prevent mixups and to ensure orderly handlings. For certain devices, additional traceability requirements apply under section 519(e) of the act and part §§ 820.65 and 820.165 of this chapter.

§ 820.65 Critical devices, traceability.

Each manufacturer shall identify each unit, batch, or lot of critical devices with a control number. Such identification shall be recorded in the device history record.

Subpart G—Production and Process Controls

§ 820.70 Production and process controls.

(a) *General.* Each manufacturer shall design, conduct, and control all production processes to ensure that a device conforms to its specifications. Where any deviation from device specifications could occur as a result of the manufacturing process, the manufacturer shall establish and maintain process control procedures that describe all process controls necessary to ensure conformance to specifications. Process controls shall include:

(1) Documented instructions, standard operating procedures (SOP's), and methods that define and control the manner of production, installation, and servicing;

(2) Monitoring and control of process parameters and component and device characteristics during production, installation, and servicing;

(3) Compliance with applied reference standards or codes and process control procedures;

(4) The approval of processes and process equipment; and

(5) Criteria for workmanship which shall be expressed in documented standards or by means of representative samples.

(b) *Environmental control.* Each manufacturer shall establish and maintain a control system to prevent contamination or other adverse effects on the device and to provide proper conditions for all operations. Conditions to be considered for control include: Lighting, ventilation, space, temperature, humidity, air pressure, filtration, airborne contamination, static electricity, and other environmental conditions. Each manufacturer shall periodically inspect its facilities and review its control system to verify that the system is adequate and functioning properly. Records of the results of such inspections shall be made and reviewed.

(c) *Cleaning and sanitation.* Each manufacturer shall establish and maintain adequate cleaning procedures and schedules to meet manufacturing process specifications. Each manufacturer shall ensure that the appropriate personnel understand such procedures.

(d) *Personnel health and cleanliness.* Each manufacturer shall ensure that personnel in contact with a device or its environment are clean, healthy, and suitably attired where lack of cleanliness, good health, or suitable attire could adversely affect the device. Any person who appears to be unclean or inappropriately attired shall be excluded from operations until he or she is clean and suitably attired. Any person who, by medical examination or supervisory observation, appears to have a condition which could adversely affect the device shall be excluded from operations until the condition is corrected. Each manufacturer shall instruct personnel to report such conditions to their supervisors.

(1) Clothing. When special clothing requirements are necessary to ensure that a device is fit for its intended use, each manufacturer shall provide clean dressing for personnel.

(2) Hygiene. Each manufacturer shall provide clean and adequate washing and toilet facilities.

(3) Personnel practices. When eating, drinking, smoking, and other activities by personnel may have an adverse effect on a device, each manufacturer shall limit such practices to designated areas. Each manufacturer shall ensure that its personnel understand any such limits. Each manufacturer shall designate selected areas to avoid any adverse effects on a device.

(e) *Contamination control.* Each manufacturer shall establish and maintain procedures to prevent contamination of equipment, components, manufacturing materials, and in-process and finished devices by rodenticides, insecticides, fungicides, fumigants, cleaning and sanitizing substances, and hazardous substances, including hazardous substances or contaminants generated by the manufacturing process.

(f) *Sewage and refuse disposal.* Each manufacturer shall dispose of sewage, trash, byproducts, chemical effluents, and other refuse in a safe, timely, and sanitary manner.

(g) *Equipment.* Each manufacturer shall ensure that all equipment used in the manufacturing process is adequate for its intended use and is appropriately designed, constructed, placed, and installed to facilitate maintenance, adjustment, cleaning, and use.

(1) Maintenance schedule. Each manufacturer shall establish and maintain schedules for the maintenance, adjustment, and, where applicable, cleaning of equipment to ensure that manufacturing specifications are met. The maintenance schedule shall be visibly posted on or near each piece of equipment or shall be readily available to personnel performing maintenance activities. A written record shall be maintained documenting the date when scheduled maintenance activities were performed and the individual(s) performing the maintenance activity.

(2) Inspection. Each manufacturer shall conduct periodic inspections in accordance with established procedures to ensure adherence to applicable equipment maintenance schedules. The inspections, including the date and individual conducting the inspections, shall be documented.

(3) Adjustment. Each manufacturer shall ensure that any inherent limitations or allowable tolerances are visibly posted on or near equipment requiring periodic adjustments or are readily available to personnel performing these adjustments.

(4) Manufacturing material. Each manufacturer shall establish and maintain procedures for the use and removal of manufacturing material to ensure that such material is removed from the device or limited to a specified amount that does not adversely affect the device's quality. The removal of such manufacturing material shall be documented.

(h) *Automated processes.* When computers are used as part of production, the quality system, or automated data processing systems, individuals designated by the manufacturer shall validate the computer software according to an established protocol. The results shall be documented. All software changes shall be made by a designated individual(s) through an established validation and approval procedure in accordance with § 820.40(c) document changes.

§ 820.75 Special processes.

(a) Each manufacturer shall ensure that special processes are:

(1) Validated according to an established protocol and records shall be made of the results of validation, including the date of and individual responsible for the validation;

(2) Conducted according to established procedures that describe all processing controls necessary to ensure conformance to specifications;

(3) Monitored according to establish procedures to ensure process parameters are met; and

(4) Performed by qualified, designated individuals.

(b) The individual(s) responsible for the performance of a special process shall record the completion of the process in the device history record. The record shall include identification of the process, the date performed, each individual that performed the special process, and the equipment used.

Subpart H—Inspection and Testing

§ 820.80 Inspection and testing.

(a) *General.* Each manufacturer shall establish and maintain the inspection and testing activities necessary to ensure that specified requirements are met. The results of all inspection and testing shall be documented.

(b) *Receiving inspection and testing.* Each manufacturer shall establish and maintain procedures for acceptance of incoming components, manufacturing materials, and finished devices. Incoming components, manufacturing materials, and finished devices shall not be used or processed until they have been verified as conforming to specified requirements. Individual(s) designated by the manufacturer shall accept or reject incoming components, finished devices, and manufacturing materials. Acceptance and rejection shall be documented.

(c) *In-process inspection and testing.* Each manufacturer shall establish and maintain procedures for inspecting and testing in-process components, finished devices, and manufacturing materials. Each manufacturer shall establish and maintain procedures for holding in-process components, finished devices, and manufacturing materials until the required inspection and tests have been completed or necessary reports have been received and verified.

(d) *Final inspection and testing.* Each manufacturer shall establish and maintain procedures for finished device inspection to ensure each lot or batch meets device specifications. Finished devices shall be held in quarantine or otherwise adequately controlled until released by an individual designated by the manufacturer. Finished devices shall not be released until all the required activities specified in the DMR have been completed and the associated data and documentation are reviewed to ensure all acceptance criteria have been met. Release, including the date and signature of the designated individual(s) responsible for release, shall be documented.

(e) *Inspection and test records.* Each manufacturer shall maintain records of the results of all inspections and tests required by this part. These records shall include the acceptance criteria, inspection checks performed; results; equipment used; and the date and signature of the individual(s) conducting the inspection and testing. These records shall be part of the device history record.

§ 820.84 Inspection, measuring, and test equipment.

Each manufacturer shall ensure that all measurement and test equipment, including mechanical, automated, or electronic inspection and test equipment, is suitable for its intended purposes and is capable of producing valid results. Each manufacturer shall establish and maintain procedures to ensure that equipment is routinely calibrated, inspected, and checked. Records documenting these activities shall be maintained.

(a) *Calibration.* Each manufacturer shall establish and maintain calibration procedures that include specific directions and limits for accuracy and precision and provisions for remedial action when accuracy and precision limits are not met. Calibration shall be performed by personnel who have the necessary education, training, background, and experience.

(b) *Calibration standards.* Each manufacturer shall establish and maintain calibration standards for measurement equipment that are traceable to the national standards of the National Institute for Standards and Technology, Department of Commerce. If national standards are not practical or available, the manufacturer shall use an independent reproducible standard. If no applicable standard exists, the manufacturer shall establish and maintain an in-house standard.

(c) *Calibration records.* Each manufacturer shall ensure that records of calibration dates, the individual performing each calibration, and the next calibration date are maintained. These records shall be maintained by individuals designated by the manufacturer and displayed on or near each piece of equipment or shall be readily available to the personnel using such equipment and the individuals responsible for calibrating the equipment.

(d) *Maintenance.* Each manufacturer shall establish and maintain procedures to ensure that the handling, preservation, and storage of inspection, measuring, and test equipment is such that their accuracy and fitness-for-use are maintained.

(e) *Facilities.* Each manufacturer shall protect inspection, measuring, and test facilities and equipment, including both test hardware and test software, from adjustments that would invalidate the calibration.

§ 820.86 Inspection and test status.

(a) Each manufacturer shall identify the inspection and test status of all components, manufacturing materials, and finished devices. The identification shall be visible, shall indicate the conformance or nonconformance of these items with respect to acceptance criteria, and shall be maintained, as necessary, throughout component acceptance, manufacturing, packaging, labeling, installation, and servicing of the device to ensure that only components, finished devices, and manufacturing materials which have passed the required inspections and tests are distributed, used, or installed.

(b) Each manufacturer shall ensure that records shall identify the individual(s) responsible for the release of components, of manufacturing materials, and of finished devices.

Subpart I—Nonconforming Components and Devices

§ 820.90 Nonconforming components and devices.

(a) *Control of nonconforming components and devices.* Each manufacturer shall establish and maintain procedures to ensure that components, manufacturing materials, finished devices, and returned devices that do not conform to specified requirements are not inadvertently used or installed. The procedures shall provide for the identification, documentation, investigation, segregation, and disposition of nonconforming components, manufacturing materials, finished devices, and returned devices, and for notification of the persons or organizations responsible for the nonconformance.

(b) *Nonconformity review and disposition.* (1) The responsibility for review and the authority for the disposition of nonconforming components, manufacturing materials,

finished devices, and returned devices shall be defined.

(2) Each manufacturer shall establish and maintain procedures for the reprocessing, retesting, and reinspection of nonconforming components and finished devices, to ensure that they meet their original, or subsequently modified and approved, specifications. The procedures shall be contained or referenced in the device master record. Reprocessed devices or components shall be clearly identified as reprocessed, and the reprocessing and reinspection results shall be recorded in the device history record. Reprocessed devices or components shall be subject to another complete reinspection for any characteristic of the device which may be adversely affected by such reprocessing. When there is repeated reprocessing of a device or component, a determination of the effect of the reprocessing upon the device or component shall be made and documented.

Subpart J—Corrective Action

§ 820.100 Corrective action.

(a) Each manufacturer shall establish and maintain procedures for:

(1) Analyzing all processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming components, finished devices, or other quality problems (analysis shall include trend analysis to detect recurring quality problems);

(2) Investigating the failure of any distributed device to meet specifications;

(3) Identifying action needed to correct the cause and prevent recurrence of nonconforming components or finished devices and other quality problems;

(4) Verifying or validating the adequacy of the corrective action to ensure that the corrective action does not adversely affect the finished device and that the corrective action is effective;

(5) Implementing and recording changes in methods and procedures needed as a result of the identification of quality problems and corrective action; and

(6) Ensuring that quality problem information is disseminated to those directly responsible for ensuring quality and is reviewed by management.

(b) All activities required under this section, and their results, shall be documented.

Subpart K—Handling, Storage, Distribution, and Installation

§ 820.120 Handling.

Each manufacturer shall establish and maintain procedures to ensure that mixups, damage, deterioration, or other adverse effects to components, finished devices, and manufacturing materials do not occur during any stage of handling.

§ 820.122 Storage.

(a) Each manufacturer shall establish and maintain procedures for the control of storage areas or stock rooms for components, manufacturing materials, and finished devices to prevent mixups, damage, deterioration, or other adverse effects pending use or distribution.

(b) Each manufacturer shall establish and maintain procedures for authorizing receipt from and dispatch to such designated areas. Any control number or other identification used shall be legible and clearly visible. When the quality of components or finished devices deteriorates over time, such devices shall be stored in a manner to facilitate proper stock rotation and their condition shall be assessed at appropriate intervals. Each manufacturer shall establish and maintain procedures to ensure that all obsolete, rejected, or deteriorated manufacturing materials, components, and devices located in storage are not inadvertently used or distributed.

§ 820.124 Distribution.

(a) Each manufacturer shall establish and maintain procedures for control and distribution of finished devices to ensure that only those devices approved for release are distributed. Where a device's fitness-for-use or quality deteriorates over time, the procedures shall ensure that the oldest approved devices are distributed first and that expired devices are not distributed.

(b) Each manufacturer shall maintain distribution records which include or make reference to the location of:

(1) The name and address of the consignee;

(2) The identification and quantity of devices shipped, the date shipped; and

(3) Any control number used for traceability.

§ 820.126 Installation.

Each manufacturer shall establish and maintain adequate instructions and procedures for proper device installation. Instructions and procedures shall include directions for verifying proper performance of the installation. When a manufacturer or its authorized representative installs a device, the manufacturer or representative shall verify that the device(s) will perform as intended after installation. The results of verification shall be recorded. When a person other than the manufacturer or its authorized representative installs a device, the manufacturer shall ensure that the installation instructions and procedures are distributed with the device or otherwise available to the person installing the device.

Subpart L—Packaging and Labeling Control

§ 820.160 Device packaging.

Each manufacturer shall design and construct device packaging and shipping containers to protect the device from alteration or damage during the customary conditions of processing, storage, handling, and distribution.

§ 820.162 Device labeling.

Each manufacturer shall establish and maintain procedures to maintain labeling integrity and to prevent labeling mixups.

(a) *Labeling integrity.* Each manufacturer shall ensure that labels are designed, printed, and, where applicable, applied so as to remain legible and affixed to the device during the customary conditions of processing, storage, handling, distribution, and use.

(b) *Labeling inspection.* Labels shall not be released for storage or use until a designated individual(s) has examined the labeling for accuracy including, where applicable, the correct expiration date, control number, storage instructions, handling instructions, and additional processing instructions. The release, including the date, name and signature of the individuals performing the examination, shall be documented in the device history record.

(c) *Labeling storage.* Each manufacturer shall store and maintain labeling in a manner that provides proper identification and is designed to prevent mixups.

(d) *Labeling control.* Each manufacturer shall control labeling and packaging operations to prevent labeling mixups.

§ 820.165 Critical devices, labeling.

Labeling for critical devices shall contain a control number.

Subpart M—Records

§ 820.180 General requirements.

All records shall be legible and shall be stored to minimize deterioration, prevent loss, and allow rapid retrieval. All records stored in automated data processing systems shall be backed up. All records required by this part shall be maintained at the manufacturing

establishment or other location that is reasonably accessible to responsible officials of the manufacturer and to employees of the Food and Drug Administration designated to perform inspections. Such records shall be available for review and copying by such employee. Except as specifically provided elsewhere, the following general provisions shall apply to all records required by this part.

(a) *Confidentiality.* Those records deemed confidential by the manufacturer may be marked to aid the Food and Drug Administration in determining whether information may be disclosed under the public information regulation in part 20 of this chapter.

(b) *Record retention period.* All required records pertaining to a device shall be retained for a period of time equivalent to the design and expected life of the device, but in no case less than 2 years from the date of release for commercial distribution by the manufacturer. Photostatic or other reproductions of records required by this part may be used. Where reduction techniques such as microfilming are used, suitable reading and photocopying equipment shall be available for use with the records.

§ 820.181 Device master record (DMR).

Each manufacturer shall maintain device master records (DMR's). Each manufacturer shall ensure that each DMR is prepared, dated, and signed by qualified individual(s) designated by the manufacturer. Any changes in a DMR shall meet the applicable requirements of § 820.40. The DMR for each type of device shall include, or refer to the location of, the following information:

(a) Device specifications including appropriate drawings, composition, formulation, component specifications, software design specifications, and software source code;

(b) Production process specifications including the appropriate equipment specifications, production methods, production procedures, and production environment specifications;

(c) Quality system documents, including verification checks used, the verification apparatus used, and validation protocols and results;

(d) Packaging and labeling specifications, including methods and processes used; and

(e) Installation, maintenance, and servicing procedures and methods.

§ 820.184 Device history record.

Each manufacturer shall maintain device history records. Each manufacturer shall establish and maintain procedures to ensure that device history records are maintained for each batch lot, or unit to demonstrate that the device(s) was manufactured in accordance with the device master record and the requirements of this part. Device history records shall be readily accessible and maintained by a designated individual(s). The device history record shall include, or refer to the location of, the following information:

(a) The dates of manufacture;

(b) The quantity manufactured;

(c) The quantity released for distribution;

(d) The labeling; and

(e) Any control number(s) used.

§ 820.198 Complaint files.

(a) Each manufacturer shall maintain complaint files. Each manufacturer shall establish and maintain procedures for receiving, reviewing, evaluating, and maintaining complaints. Such procedures shall ensure that:

(1) Complaints are received, reviewed, evaluated, investigated, and maintained by a formally designated unit;

(2) Oral complaints are documented upon receipt; and

(3) The complaint is reviewed to determine whether an investigation is necessary. When no investigation is made, the unit shall maintain a record that includes the reason no investigation was made and the name of the individual responsible for the decision not to investigate.

(b) Each manufacturer shall review, evaluate, and investigate all complaints involving the possible failure of a device, labeling, or packaging to meet any of its specifications. Any complaint pertaining to death, injury, or any hazard to safety shall be immediately reviewed, evaluated, and investigated by a designated individual(s) and shall be maintained in a separate portion of the complaint files. Investigations shall include a determination of whether there was an actual device failure to perform pursuant to specifications; whether the device was being used to treat or diagnose a patient; whether a death, injury, or serious illness was involved; and the relationship, if any, of the device to the reported incident or adverse event.

(c) When an investigation is made, a written record of each investigation shall be maintained by the formally designated unit identified in paragraph (a) of this section. The record of investigation shall include:

(1) The name of the device;

(2) The date the complaint was received;

(3) Any control number used;

(4) The name, address, and phone number of the complainant;

(5) The nature of the complaint; and

(6) The results of the investigation.

(d) The investigation results shall include:

(1) The corrective action taken;

(2) The dates of the investigation;

(3) The details of the complaint; and

(4) The reply to the complainant.

(e) When no reply is made to the complainant, the reason shall be recorded.

(f) Records of investigations of events that are determined to be reportable under medical device reporting (MDR) requirements of part 803 of this chapter shall include the information required by part 803 of this chapter. When such information cannot be obtained, a record of the reason shall be made and retained in the record of investigation.

(g) When the formally designated complaint unit is located at a site separate from the actual manufacturing establishment and a complaint involves the manufacturing site, a duplicate copy of the complaint and the record of investigation of the complaint shall be transmitted to and maintained at the actual manufacturing establishment in a file designated for device complaints.

(h) If a manufacturer's formally designated complaint unit is located outside of the United States, a copy of all of each records required under this section shall be maintained in the United States. If a manufacturer has a location in the United States where records are regularly kept, the copies required under this paragraph may be maintained at such location. Otherwise, the copies required under this paragraph shall be provided to and kept by the agent designated under § 803.26(g)(3) of this chapter.

(i) Each manufacturer shall establish and maintain procedures for processing complaints to ensure that all complaints are processed in a uniform and timely manner. Such procedures shall include provisions for determining whether the complaint represents an event which is required to be reported to the Food and Drug Administration under part 803 of this chapter.

(j) Any written or oral complaint that is also a reportable event under part 803 of this chapter shall be identified in the complaint file as such.

Subpart N—Servicing

§ 820.200 Servicing.

Each manufacturer shall establish and maintain procedures to ensure that finished devices that are serviced by the manufacturer or its representatives meet specifications. Procedures for servicing

shall include provisions for determining if service requests represent an event which must be reported to the Food and Drug Administration under the requirements of part 803 of this chapter.

(a) *Service records.* Each manufacturer shall establish and maintain procedures to ensure that service records are maintained that identify the device serviced, including any control number used, the date of service, the service performed, and individual(s) servicing the device.

(b) *Service record evaluation.* Each manufacturer shall analyze servicing records in accordance with § 820.100; except that when a service report involves a death, serious injury, or safety hazard, the report shall be considered a complaint and shall be investigated in accordance with the requirements of § 820.198.

Subpart O—Statistical Techniques

§ 820.250 Statistical techniques.

(a) Where appropriate, each manufacturer shall establish and maintain procedures for identifying valid statistical techniques required for verifying the acceptability of process capability and product characteristics.

(b) Sampling plans shall be written and based on a valid statistical rationale. Each manufacturer shall establish and maintain procedures to ensure that sampling methods are adequate for their intended use and are regularly reviewed, especially for events such as nonconforming devices, adverse quality audit reports, or complaints.

Dated: October 15, 1993.

Michael R. Taylor,

Deputy Commissioner for Policy.

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